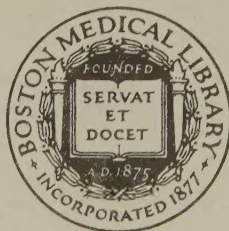


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THE THERAPY OF PUERPERAL FEVER



# THE THERAPY OF PUERPERAL FEVER

BY

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VIENNA, AUSTRIA

AMERICAN EDITION

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ST. LOUIS

*WITH TWENTY-SEVEN ILLUSTRATIONS*

ST. LOUIS  
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## PREFACE TO AMERICAN EDITION

Many efforts, in various directions, are at present being made in this country to reduce the appalling death rate from puerperal infections. Any addition to our knowledge, which is likely to aid in amending a situation that fairly discredits obstetric science, must be welcomed by the profession. This is the reason and explanation for my ready consent to prepare an American edition of Koehler's monograph: *Die Therapie des Wochenbettfiebers*.

To my best knowledge no work dealing specifically with the problem of puerperal infection has been presented to the English speaking physicians within the last fifteen years. During this time, however, the utter futility of many of the older therapeutic measures, medicinal and surgical, has been established and newer methods have been proposed and sponsored. The treatment of systemic infections by means of antiseptic solutions directly infused into the blood stream, chemotherapy and, most important of all, nonspecific protein therapy, all very recent additions to our general therapeutic armamentarium, have been introduced as well into the treatment of puerperal fever. With what success? Koehler endeavors to furnish a reliable answer to this obvious and important question.

In the abundant material of the obstetric-gynecologic clinic of Professor Josef Halban of Vienna, Koehler found an opportunity, offered to only few American gynecologists, to test many of the novel suggestions. Autopsies, which in Continental hospitals are about as much the rule as exceptions with us, enabled him not only to study in a large number of cases the exact pathologic conditions responsible for the patient's death, but also to judge whether and how the employed therapy had helped, or what other method might have proved more useful.

Thoroughly familiar with literature and endowed with a critical mind, Koehler is well fitted to analyze judiciously the innumerable therapeutic suggestions that have been made of late—often apparently not to the ultimate benefit of the women suffering from puerperal infections. He proves himself entirely out of sympathy with the dangerous enthusiast who advocates a questionable procedure before it is securely tested. He is not pessimistic, but practices a healthy skepticism.

This volume reflects the rational and impartial judgment of an experienced physician and, therefore, I am willing to recommend its careful study to the American profession.

HUGO EHRENFEST.

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## INTRODUCTION

The high puerperal mortality of the past, still too high in spite of considerable progress, readily explains the great variety of therapeutic methods that have been advanced in the effort to reduce the risks of puerperal infection. Unfortunately we must admit that the achieved success does not correspond to the devotion and ingenuity spent in these efforts.

The most conspicuous evidence of the failure to solve the task might be found in the multiplicity of contributions in all languages of the world, dealing with the Therapy of Puerperal Infections. It is another example of the truism that the positive value of theoretical propositions stands in an inverse ratio to their number.

Without the slightest doubt in the honesty and good will of the authors one cannot escape the conviction that many of them have been carried away by unwarranted enthusiasm. Were it not so, one could not understand why, with so many excellent curative methods at our disposal, women still are dying of puerperal infections.

This overproduction of partly baseless therapeutic suggestions undeniably is responsible for the existing meddlesomeness which proves far from advantageous to the patients. Nevertheless we must appreciate how the physician in his anxiety to help, when meeting failure with a well-established procedure, will all too willingly turn to another remedy, still far from having proved its value. If by a fortunate, or better, by an unfortunate coincidence this patient recovers, this seeming success all too often is quickly published and thus grows steadily the number of agents "effective in even the most desperate case."

Judgment concerning the actual value of a certain procedure or remedy, however, can be granted only to him who

by extensive experience has learned that many a seemingly light case of puerperal fever will be lost in spite of the employment of the best of recognized methods of treatment while another infected puerpera will recover though the gravity of the symptoms justified a well-nigh hopeless prognosis, so that for this very reason possibly, use was made in this instance solely, of a few merely symptomatic measures.

It thus is not surprising that the clinical observation of a large number of cases of puerperal sepsis finally will lead to the realization of one's utter helplessness. At first thought this must seem surprising. We are able to discern the etiologic factor of the disease, often the responsible germ, the mode of infection, the port of its entrance, the path along which it is spreading, and all this information should be sufficient for adequate efforts of therapy. But as in relation to other diseases, we must realize that also in puerperal infection satisfactory curative results obtained in animal experiments cannot be duplicated at the bedside of our patients.

The biologic reactions of bacteria in the test tube are very different from those in the living organism, and again different in the artificially infected, but otherwise healthy, animal from those observed in the sick puerpera. The modes of infection are dissimilar and so are the possibilities for the further extension of the process.

The experimental animal does not offer the favorable factors for rapid multiplication of bacteria in form of bruised or necrotic tissues and large blood clots, present in the woman immediately after delivery. Usually infected by subcutaneous or intraperitoneal injection, the animal hardly ever develops thrombotic processes which in the puerperal woman are so common and represent the chief source for the later establishment of metastatic foci.

In contrast to the animal employed in an experiment the resistance of the puerpera is greatly reduced by the strain

of labor, by the loss of blood, etc. Therefore in our specific problem therapeutic success in the laboratory with a certain remedy really means nothing for the clinician.

This holds true even for experiments in which the infection is produced in an animal immediately after labor, as has been done, e.g., by Mayerhofer. By injecting putrid blood into the uterus of a puerperal rabbit he succeeded in generating solely an endometritis and never a general infection, to say nothing of a thrombotic process. Certain preliminary conditions are missing. There is no retention of placental elements or of coagula. The fetuses had been expelled quickly without noteworthy injury, without strain, and without operative help—a factor deserving special emphasis. There are specific differences in the constitution of the endometrium. In the rabbit within a few hours postpartum, in the horse within a few days, the endometrium is completely restored as proved by the possibility of a new impregnation at that time. In woman, regeneration of the endometrium requires a long time. The exact mode of infection that in a woman leads to puerperal fever cannot be reproduced in the animal.

These evident facts do not only explain existing and obvious difficulties in the successful treatment of puerperal sepsis but necessarily also prove discouraging in any attempt to offer a thorough and critical analysis of this complex problem of therapy. Nevertheless I venture to undertake the task. Careful observation of large series of cases in regard to seeming influence exerted by many of the better known measures and by others devised by myself, and exact control of effect or more often of failure of these measures at autopsy in very many instances, I trust, will justify my effort.

The volume of available material and existing literature make it impossible to offer a truly exhaustive survey. I also shall refrain from proving or disproving the value of this or that remedy by means of statistics. It shall be my



task to set forth comprehensively the various therapeutic measures and remedies and to state precisely the results of our own experience with each, elucidating important facts by citation of the clinical histories of certain particularly characteristic cases.

Statistical figures prove of no value in the problem of puerperal fever. In this disease too many unmeasurable quantities such as virulence of the germ, resistance of the patient, or cardiac function enter into the question of prognosis. They determine the final outcome to such an extent that the impossibility of their statistical consideration must unavoidably annul the relevancy of any conclusions concerning the efficacy of the therapeutic measure resorted to, if based solely on percentage figures of recoveries or deaths.

# THE THERAPY OF PUERPERAL FEVER

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## PART I. PROPHYLAXIS

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### CHAPTER I

#### PROTECTION OF THE PATIENT

More important than its cure always is the prevention of a disease. It would transgress the scope of this volume to quote here all the measures that have been proposed for the prevention of the infection of a patient, either ante- or intrapartum. Many of them certainly possess very limited if any value. I am far from accepting the nihilistic attitude of those who are satisfied that "millions of women among the savage races pass unharmed through childbirth," but I cannot hesitate to express it as my belief that some of the modern obstetric clinics certainly go too far in the matter of prophylaxis. Excessive zeal in this respect is not free of possible dangers.

To be sure, a clinic in which internal examinations, often repeated for the benefit of students, unavoidably increase the risk of infection, will be forced to institute special protective precautions. This practice, however, does not yet prove the expediency of extravagant prophylactic procedures. Comparison does not reveal for such clinics any noteworthy better results in regard to the incidence of puerperal mortality or morbidity. This permits the deduction that smaller institutions, not employed for instruction of students or midwives, and especially the practitioner, are justified in making use of a less cumbersome prophylaxis.

lactic technic as long as they will not omit those features which today are generally regarded as imperative in modern obstetric practice.

All protective measures must take into account the two possible sources of infections, those lying outside the patient and those existing within the birth canal. Definite difficulties are experienced in the elimination of either source. With reliable sterilization of instruments, dressings and linens, as easily procured in every good hospital, the problem rests with proper disinfection of the hands of physician or midwife, and the proper preparation of the birth canal.

### Disinfection of Hands

Much thought has been bestowed on the problem of reliable hand disinfection ever since the importance of this factor has been duly appreciated, which really means, ever since the true meaning of Semmelweiss's observations was fully understood.

The most favored procedures have remained the methods of Ahlfeld (hot water and alcohol) and of Fuerbringer (hot water, alcohol and bichloride). They have stood the test of long experience. However, it must be admitted that either of them accomplishes only a reduction but not a complete elimination of germs from the hands.

Absolute sterility of the hands cannot be obtained by any known method. This has been conclusively shown by various investigators and also in my own experiments made with Dr. Hecht in the First Surgical Clinic at the University of Vienna.

In our studies we poured at various intervals during scrubbing 5 c.c. of sterile bouillon over our hands, rubbed them with the fluid, and inoculated agar tubes with one c.c. of this fluid. Also our investigations demonstrated that washing in hot water after a short while causes a reduction

in the number of microorganisms but never absolute freedom of them. Long-continued washing, however, actually produced again a marked increase in the number of colonies. The hot water and the brush led to this surprising and undesirable effect because they brought many of the bacteria, lying in the depth of the skin, to the surface.

Short washing with brush of the scrubbed hands in alcohol (between one-half and one minute) reduces the number of germs. If continued for three or four minutes in a running stream of alcohol, the procedure results sometimes in seemingly perfect sterilization, while in other tests only a diminution of germs could be ascertained. Washing in alcohol, without a preceding scrubbing in hot water, after three minutes will cause a striking reduction in the number of colonies.

The method of Gibson (rubbing the hands with a small amount of calcium chlorate and caustic soda in warm water and rinsing in sterile water) has the advantage of speed, but the disadvantage of harming the skin, and of the disagreeable smell of chlorine.

With the impossibility of reliable sterilization of the hands themselves definitely established, the necessity becomes obvious of covering them with some material that can be sterilized.

### Gloves

Gloves made of lisle thread or of rubber have been recommended.

The lisle thread glove offers but little advantage. It can be maintained sterile only as long as it is dry. When becoming moist, it permits germs to enter, but as shown by my own experiments as well as those of Helle, even then it affords a certain amount of protection since the germs are retained within its texture. Repeated changing of these gloves in the course of operation therefore is indispensable.

Supreme protection both for physician and patient is

offered by the intact sterile rubber glove. Whatever doubt there existed concerning its utility was fully dissipated by experience gained in the war. The usefulness of the rubber glove in the prevention of septic infection today stands unchallenged.

During the war practically every obstetrician in Austria and Germany was forced to manage also many thoroughly infected surgical patients. There was no possibility of the customary division of clean from septic cases in the hospitals. It was the use of the rubber glove which prevented during the war any noteworthy increase of either mortality or morbidity of the puerperium.

It had been claimed that sweating of the gloved hand causes the accumulation of many bacteria, which when suddenly released by accidental injury to the glove actually increase the chances for infection of the patient. However, my own studies showed that even then decidedly fewer germs will reach the wound than would have been introduced from the total surface of the unprotected hand.

The only objections that might be raised against the rubber glove are its vulnerability and its excessive price—at least under present conditions in Middle Europe. Neither objection counts in the face of the wonderful advantages it offers.

Concerning other protective schemes, such as covering the hands with a layer of chirosoter,<sup>1</sup> gaudanin,<sup>2</sup> or dermagummit,<sup>3</sup> I cannot pass judgment, since I made relatively few experiments with them. However, they solely reduce the chances of infection but do not procure sterility, and unfortunately these thin covers crack and tear easily. They furthermore prove rather irritating to the skin.

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<sup>1</sup>A solution of balsam- and wax-like substances in carbon tetrachloride.

<sup>2</sup>Paragum dissolved in forman-benzine to which forman-ether is added to a formalin concentration of 1 per cent. The substance is soluble in ether, benzine and chloroform.

<sup>3</sup>Closely resembles gaudanin.

These three preparations are painted on the skin of the field of operation or on the hands of the operator, where on drying they form a thin, elastic cover which prevents egress of the microorganism in the skin.



Better than with any specific method of hand disinfection can we protect the woman in labor by preventing, as far as possible, our hands from coming into direct contact with infective material. Obviously in practice this precaution, however desirable, cannot be fully achieved, not even by the specialist. For this reason alone the use of rubber gloves becomes indispensable, since it precludes the contamination of the obstetrician's hands with pathogenic germs. The "prophylactic" prophylaxis of employing rubber gloves for every examination and in the management of all infected cases today represents the best available method of prevention of puerperal fever.

### **Rectal Examination**

Among prophylactic measures, routine examination through the rectum during labor holds an important place. This method was first recommended, about twenty years ago, by Kroenig and Thiess. It found but few advocates and was practically forgotten until its employment more recently again has been propagated by some, especially American obstetricians. Its precise value is still under dispute and, as a matter of fact, rectal examination during labor is mentioned in but a few of modern textbooks of obstetrics, and if at all, usually only with a few words. There can be no doubt that this method of exploration offers certain advantages. It precludes the possibility of carrying vaginal germs into the cervix and uterus as is inevitably done in the customary vaginal examination. A rectal exploration can be made quickly because it eliminates time-consuming scrubbing of the hands. This is a factor of importance in a larger obstetric clinic when several cases in labor have to be managed simultaneously. These benefits, in part at least, are counterbalanced by such shortcomings of the method as possibility of transference of intestinal bacteria to the perineum, or of contamination of the finger

of the examiner. Both these possibilities are of no particular consequence. Contamination of the perineum with fecal matter often cannot be prevented when the head passes through the vulvar ring and usually proves innocuous. A good heavy glove will not tear, and if it does, the hand must immediately be thoroughly cleaned.

Of more significance is the fact that rectal examination never permits the accuracy of palpatory findings obtained by vaginal exploration. The thickness of the interposed tissues (the septum rectovaginale) often prevents one from making out certain details, e. g., the state of the amniotic sac, especially if not well filled, or the presenting edge of the placenta, a prolapsed cord, etc. This is particularly true when the presenting fetal part is still high and thus does not act as a fixed back rest against which the object to be palpated can be pressed.

Experience with the method enables one to diagnose with sufficient accuracy the condition of the cervix, the direction of sutures or location of fontanels.

In my opinion it is unjustifiable to repudiate rectal examination on principle. If it does not prove satisfactory in the individual case, a vaginal examination always can be added, but very often it will obviate the necessity of the certainly more dangerous vaginal exploration. The method should be taught all students.

### **Preparation of the Parturient**

This preparation is of no less importance than the appropriate preparation of the physician's hands.

### **Bath**

The question of bath has been extensively discussed. With the amniotic sac intact and birth channel only slightly dilated, the tub bath certainly can do no harm and therefore can be recommended without hesitation especially for

the clinic, which deals with women not all too clean as a rule. Experiments with dyes dissolved in the bath water (Zweifel) have shown that in the tub, bath fluid, and with it of course also bacteria, might penetrate deeply into the vagina up to the fornices. This would cause not only the introduction of infectious material but likewise the dilution of the normally bactericidal vaginal secretions. Therefore it will be preferable in advanced labor to refrain from the tub bath and to limit the cleansing to washing of the external genitalia, or to make general use of the American practice of cleaning all parturient women standing up in the tub under a spray shower. Obstetricians who forbid all bathing for several days before expected labor undeniably go too far. The clipping or shaving of the pubic hair is advisable.

### Vaginal Douching

Douches with lysol, lysoform or a similar disinfectant certainly can do no harm, but, on the other hand, their efficacy must not be overestimated. At best they effect solely the mechanical removal of a part of the germ-laden vaginal discharge, but they never really act as germicides. The entire effect soon passes off. Not causing actual destruction of truly virulent microorganisms, antiseptic douches can be dispensed with, since the saprophytic bacteria of the vagina, as a rule, prove harmless. Douches might be of limited benefit immediately antepartum when combined with careful scrubbing of the vagina, but then only if the mechanical cleaning actually has not caused even small lesions of the surface epithelium. Otherwise this presumably protective procedure is likely to do more harm than good.

Deserving of a more detailed discussion are prophylactic douches with a lactic acid solution. They were recommended by Zweifel and Schweitzer and are based on newer information concerning the germ flora and chemistry of

the vagina. We now know that normally the chemical reaction of vaginal secretions is acid, and that pathologic processes will reduce their acidity or even render them alkaline.

This acid reaction is dependent upon the presence of lactic acid produced in the vagina through fermentation of the glycogen of the epithelium by the Doederlein bacillus, normally present in the vagina (Zweifel). Only continued formation of new acid will maintain the acid concentration at its normal average level of between a half to one per cent. Physiologic conditions within the vagina both in regard to its chemical and bacterial status are determined by this acid titer. This acid concentration today is generally regarded as the sovereign prophylactic against the implantation of pathogenic germs. As a rule, it prevents multiplication of such bacteria and protects the vaginal epithelium against their invasion.

Zweifel and Schweitzer endeavored to strengthen the autoprotective ability of the vaginal mucosa, and thus to reduce the risk of infection, by employing lactic acid douches for ten days before confinement. The method has met with much approval, but also has been repudiated, e.g., by Traugott, Eisenreich, and others.

My personal experience is too limited to permit me to pass final judgment on it, but I shall mention a few of the arguments one might raise against the routine use of these lactic acid douches in obstetric work.

Though it is possible to increase with them the acid reaction to its physiologic level of one per cent, this optimum cannot be maintained very long. With the rupture of the membranes, the escaping amniotic fluid will unavoidably promptly reduce the acidity, and it will be further lowered when blood passes through, or collects in, the vagina. The alkalinity and the particular suitability of blood to act as a culture medium for bacteria of any kind will quickly



void any protection obtained by the acid douche. After all, the ascension of vaginal bacteria, outside of manipulations, is in the main hastened by perineal or cervical injuries and the presence of retained portions of the membranes hanging down through the cervix. The requirement of employing these douches for ten days preceding labor furthermore makes their possible benefits available only to a very small percentage of all parturient women.

In consideration of all these facts very little can be expected from prophylactic douches and, as a matter of fact, some American authors (e.g., Cragin) have recorded better results without prophylactic douches in comparative series.

Obviously the situation is entirely different when operative interference is anticipated. In such cases necessarily the genitalia must be prepared just like for any other kind of operation.

In this preparation very little effect can be expected from mere washing with warm water. Our customary method of preparation consists in cleansing of external genitalia with benzine, repeated three times, followed by the application of tincture of iodine, and wiping out of vagina with a sponge soaked in benzine or alcohol, likewise repeated three times. American clinics seem at present to give preference to washing, both of external genitalia and vagina, with soap and water, removal of the soap with sterile water and application of a 5 per cent solution of picric acid in 95 per cent alcohol. The ability of benzine to dissolve the fat covering the skin enables the iodine to penetrate more deeply. In this respect the benzine-iodine mixture of Haeusner proves less effective since my experiments showed germs in large numbers on the skin even after one minute of its application.

The sole application of tincture of iodine, extensively used by surgeons since its introduction by Grossich, offers insufficient protection. Kutscher, Hecht and I have shown that bacteria even after lengthy contact with the

tincture will grow luxuriantly on a culture medium, thus proving that the tincture is not a trustworthy bactericide. The only value of the tincture is found in its ability to toughen tissues and thus to fix its bacterial contents. This effect is extended to greater depth by a preceding application of benzine. This same effect can be obtained as well with ether.

A method which yielded ideal results in our bacteriologic tests, i.e., cleaning with a half per cent solution of bichloride in alcohol, unfortunately is not applicable in obstetric work since bichloride in this high concentration through resorption might prove disastrous.

An antiseptic douche, in spite of its brief effect, will have some advantage if given immediately before an operation. The attained reduction of the germ contents of the vagina will persist during the operation. This assumption is supported by the observation of Esch and Schroeder that the identical result can be obtained also by a mere saline douche and will last from eight to twelve hours. They, therefore, agree that in the use of an antiseptic douche its disinfectant qualities are of less importance than its mechanical effect in removing germ-laden discharge.

Special risks in regard to subsequent puerperal infection are encountered in the presence of ulcerative processes on the external genitalia, vagina or cervix which practically preclude sufficient sterilization. We are using the thermocautery on furuncles or other abscesses as a preliminary procedure, and then cover the scab with sterile gauze. This procedure has proved very satisfactory in our hands.

Excessive edema, debarring the possibility of thorough cleaning, might force one to resort to a cesarean section, and gangrene of the vulva in some instances has necessitated a Porro operation (Hoehne).

Especially troublesome are infected areas in the vagina or on the cervix, often so small that they are overlooked,



at other times of such a nature that their elimination becomes an impossible task.

I remember a case in which a pulmonary tuberculosis forced us to induce an abortion, which was done under strict aseptic precautions. A few days later the patient died of a fulminant sepsis. As the primary source of infection a minute ulcer of the portio was discovered from which the hemolytic streptococcus was grown in pure culture.

There is another case in my mind, a woman in the eighth month of pregnancy. A luetic sore was discovered on the cervix which did not clear up even after the administration of several injections of neosalvarsan. At the time of labor, which occurred five weeks before term and terminated spontaneously without any internal examination, the ulcer was about two cm. in diameter, with an uneven, dirty looking base, from which various bacteria including a streptococcus were cultured. Temperature rose to 40° C. two days postpartum and persisted for twelve days. Patient finally recovered.

With observations of this sort in mind one may well feel some doubt concerning the reliability of prophylactic local measures.

## CHAPTER II

### PROPHYLACTIC IMMUNIZATION (VACCINES AND SERA)

Not too much could be expected from a prophylactic immunization by means of vaccines or sera against infections of this sort. Some time ago they had been extensively employed by Bumm, Polano, Watters and Eaton, Levy and Hamm, and others, more recently tested by Joetten. The latter prepared a vaccine from six different strains of streptococci, obtained from cases of puerperal sepsis. Briefly described his method is as follows: Centrifugation of a twenty-four hour culture grown in 1 per cent glucose bouillon. After removal of top layer, the sediment is washed several times in saline solution. Bacteria are killed, fluid tested for sterility, and germs counted. Further dilution with saline to obtain a definite germ concentration (between 25 and 500 millions to one c.c.). The obtained results were calculated by Joetten according to the number of febrile cases and deaths, and were controlled by serologic tests. Every elevation of temperature above 38° C. (in axilla) was counted as fever. Among 819 cases that had received vaccine (25 to 50 millions bacteria) 16 per cent ran a febrile course. In 433 cases receiving 100 millions of bacteria the percentage of febrility was only 13.3; in 300 cases after injection of 250 millions of bacteria it was 10.66 per cent, and in a final series of 126 patients with an immunizing total dosage of 500 millions of bacteria the morbidity fell to 7.1 per cent. In all these cases there were 5 deaths, with 4 of them in the first series. Joetten from these findings felt justified to draw the conclusion that the day of successful immunization against streptococcal infection cannot be far distant.

More recently Louros expressed similar favorable views concerning prophylactic vaccination of pregnant women. He made use of a vaccine prepared from nine strains of streptococcus, containing 500 millions bacteria in each cubic centimeter, sufficient, in his opinion, to afford protection for one month or more.

If there is sufficient time Louros gives one-half c.c. about 20 days before expected labor, and 10 days later injects a whole c.c. If the opportunity for immunization is offered only immediately before confinement, he combines the injection of 1 c.c. of the vaccine with the introduction of 50 c.c. of streptococcus serum, a method first introduced by Lorenz into veterinary medicine, but later found equally useful in parturient women by Levy and Hamm.

In this manner Louros claims to have not only reduced to a marked degree puerperal morbidity but also to have obtained good curative effect in cases already infected.

These efforts had been preceded years ago by prophylactic injection of antistreptococcus serum at a time when serum therapy still was in great favor. However, they had never proved of much value in reducing the incidence of puerperal mortality and morbidity.

Obviously the number of cases that have been treated with vaccines is too small to permit conclusive deductions concerning the value of the method, but as far as the simultaneous injection of vaccine and serum is concerned at least one definite shortcoming cannot be denied. Outside of possible immediate untowards effects, such as serum exanthema, headache, joint pain, etc., the prophylactic serum injection practically eliminates the chance of using serum later for curative purpose on account of the danger of an anaphylactic shock.

Though this particular objection does not apply to the employment of vaccines, vaccinothrapy of necessity can be beneficial only to a negligibly small percentage of parturient women. Granted the specificity of this therapy, an

assumption which is rather doubtful in itself, it would afford protective effect solely for a streptococcus infection but none for infection with any other microorganism. Protective vaccination with all the organisms that might possibly start a puerperal process is impossible in practice. Furthermore, any method of this sort would be applicable only to patients under prenatal care, that is, to women who in general are enjoying better hygienic and other protective supervision both during pregnancy and labor. It could not benefit those in greatest need of such prophylactic care, that is, patients seen for the first time in unhygienic surroundings in their homes, usually only after labor actually has started. Prophylactic and curative methods to be truly useful must be so devised that they can be carried out in general practice.

For the sake of completeness I shall briefly mention the experiments of Krol though made only on animals and never tested clinically. Large doses of mercury seemingly produced an immunization against streptococcus infection but revealed no persistent protective action. The method is based on the observation that luetics while under active treatment with mercury apparently exhibit a striking resistance against infections of all kind.

## PART II. THERAPY

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### CHAPTER III

#### GENERAL THERAPY

If we assume that the various clinical manifestations of a puerperal infection, on the one hand, represent pathologic conditions produced by the pathogenic organisms (endometritis, thrombosis, lymphangitis, metastatic abscess, etc.), and on the other hand, are reactions of the body to the infection (fever, chills), then the two directions, which all therapeutic efforts will have to take, are well defined.

We must attempt to prevent pathogenic germs or possibly their toxins from entering the body (prophylaxis) or if it is too late for that, we must attempt to destroy those already in the organism. This can be accomplished either by the administration of certain remedial substances or by mobilization or actual increase of the protective elements forming in the body (etiologic therapy). It is a further task of great importance to aid the patient in her fight against the infection by relieving actual pain and distress, and lessening the reactive symptoms (symptomatic therapy).

Later pages will show to what degree efforts in these various directions have proved successful.

It seems most suitable to discuss first, general therapeutic measures, to speak next of the results obtained with customary local therapy, to explain the various possibilities of surgical interference, and to conclude the presentation of my material with a consideration of medicinal treatment



more particularly in cases in which the infection has become systemic. I shall endeavor to state precisely, in regard to every question, the opinion I have formed from personal experience with each remedial procedure.

For the first few days postpartum, in the absence of any signs of infection or even after a rise in temperature, the physician best follows a middle course between prophylactic and therapeutic measures. Care is taken that lochial discharges do not become obstructed. The patient is properly nursed, cleaned and fed. If necessary, medicines are ordered likely to improve her general condition, to strengthen heart action or to reduce temperature.

### **Treatment of Lochial Retention**

While it is natural to let patient and uterus severely alone as long as the puerperium is progressing normally, it is not less plain that at the very onset of the symptoms of an infection seemingly originating in the uterus everything must be done to expedite the elimination of the noxious uterine contents. The first task is to secure unhindered discharge of the lochial secretions. While in many instances the mere raising of the head end of the bed (Fowler position) or keeping the patient lying on her face several times a day, will be sufficient for the purpose, in other cases drugs will have to be administered which cause the uterus to contract and thus further its involution. Various drugs are available, e.g., ergot preparations, quinine or strychnine, given hypodermically or by mouth. Batermann recommends a combination of ergot and quinine. Ovary prefers the salicylated quinine. Mack Lacklin advocates the Niemeyer mixture of opium, digitalis and quinine.

We obtained eminently satisfactory results with subcutaneous injections of various ergot preparations, and with



quinine bihydrochloricum given intramuscularly. More recently we were greatly pleased with the effect of gynergen, a water-soluble salt of the secale extract ergotamin (Spiro and Stoll). It is a very effective remedy even in the small dose of 0.1 to 0.2 mg., given subcutaneously, and only in somewhat larger doses by mouth. Larger amounts, especially in the form of hypodermic injection, are likely to cause vomiting or diarrhea.

As a rule we fortify the effect of such drugs by the application of an ice bag to the lower abdomen. For reasons, which I shall give later, we refrain from the use of hot or very cold vaginal douches for the purpose of stimulating uterine contractions. Practically never were we forced to relieve a lochiometra by means of a drainage tube.

Hypophyseal or other organ extracts by themselves are of very limited value since their effect is fleeting and never very marked on the non-pregnant uterus. These extracts, however, at times yield splendid results in the combination with ergot.

Drenkhahn suggested to tranquilize the uterus by a few doses of atropin. sulphuricum (0.5 mg.) since in this way the further spread of the infection is prevented or at least retarded. He thinks that cessation of all further uterine contractions also checks toxic resorption from the uterus.

### General Care

It seems superfluous to emphasize the necessity of good bodily care but I must point out in this connection that we object to the use of the cold tub bath for patients suffering from a puerperal infection. In spite of all precautions this procedure requires manipulations incompatible with the essential requirement of rest for the patient. It is likely to do more harm than good. The identical antipyretic effect can be obtained with the much simpler cold pack or cold sponge, to be repeated as required by conditions.

### Antipyretics

Opinions are divided as to the propriety of the employment of antipyretics. While, for example, v. Rosthorn or Burtenshaw object to them on principle, others urgently advocate the use of such remedies as quinine, phenacetin, salicyl, antipyrin, and more recently of pyramidon.<sup>1</sup>

No objection can be raised against the use of antipyretic drugs as long as we understand that the fever is not the disease itself, but only a symptom—as is not fully realized by laymen and an occasional midwife. We solely attempt to alleviate the patient's discomfort, and benefit her by a limited reduction of her elevated temperature.

It is our rule, however, to disregard at first the fever so as to obtain a clear picture of the temperature curve and to resort to antipyretic procedures or remedies only later whenever the rise is excessive.

The particular remedy is selected in accord with certain indications. We give preference to pyramidon (0.6 to 1.0 gm. per day) in approximately 150 c.c. of fluid, divided for an hourly dose of one tablespoonful, or given in tablets, each containing 0.1 gr. We regard pyramidon not only as an antipyretic, but as an anesthetic and sedative as well, so that it is a remedy par excellence to make the patient feel better.

If we suspect lochial retention we favor quinine, given in a dose of 0.5 gm. several times a day for the purpose of stimulating uterine contractions. Often we have administered quinine intramuscularly or intravenously, counting on a possible disinfecting effect. However, this latter assumption was not supported by more extended observation as I shall point out later on.

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<sup>1</sup>Pyrazolonum dimethylaminophenyldimethyllicum. White, in water-soluble crystals. It is a derivate of antipyrin and has a similar action, but it has a more marked analgesic effect. Temperature falls slower but effect lasts longer. Cardiac and vascular diseases are strict contraindications against its use. Occasionally the remedy causes nausea, vomiting, collapse, cyanosis or exanthema, especially in patients who have a marked idiosyncrasy against this drug.

Other authors have other favorites. Charles recommended a mixture of quinine sulphate and sodium salicylate, Komor pyrenol,<sup>2</sup> while Hahn preferred atophan<sup>3</sup> which in our hands failed to show any noteworthy advantages. We also utterly failed to confirm the claim that antipyrin has an antitoxic effect. MacKay attempted to stop chills by a transfusion of 100 c.c. of blood with 200 c.c. of saline solution. The rationale of this procedure is not clear since the parenteral introduction of any foreign protein, a factor inherent to his method, by itself usually causes chills.

Unfortunately external conditions and hospital construction offer us no opportunity to test solarization and open air treatment so extensively employed in America. For this treatment is claimed not only an antipyretic and antiseptic effect but also vigorous general stimulation of the septic patient.

### Roborants

The advantage of a nutritive diet (milk, eggs, meat juice, etc.) and of the various predigested foods on the market is obvious. During the febrile stage and particularly during convalescence we prescribe some of the common arsenic-iron preparations, usually in the form of hypodermic injections, so as not to interfere with the appetite which often is already reduced. Oddi recommended a mixture of sodium salicylate (2.0 gm.), 10 per cent iron chlorate (4.0 gm.), glycerin (10.0 gm.) in distilled water (125 c.c.), one tablespoonful every two hours. We have occasionally employed this mixture which is supposed to have not only an antipyretic and tonic but also an antiphlogistic effect, the

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<sup>2</sup>A product obtained by melting acidum and sodium benzolcum, sodium salicylicum and thymol. White powder, soluble in water. It causes temperature to fall without sweat and does not affect the circulatory system. Rarely it causes vomiting.

<sup>3</sup>Formed by the addition of four parts of quinolin-carbonic acid to two parts of phenyl-carbonic acid. Crystals of bitter taste, not soluble in water, soluble in alkalis. Newer preparations, like paratophan, isatophan and novatophan are less likely to cause gastric discomfort, vomiting, exanthema or renal irritation.

latter of possible value in the presence of exudate in pleura or joints.

### Cardiac Tonics

Of greatest importance is sustenance of cardiac function since in the long drawn out case the myocardium is bound to be harmed, if not completely paralyzed, by the inundation of the body with bacteria or their toxins. For reasons already mentioned, we do not make use of the tub bath for the purpose of heart stimulation. Therefore, we prefer in general the cardiac tonics usually employed: camphorated oil, caffein and the various digitalis preparations. Also tincture of strophantus has its advantages. While not actually a tonic, strychnin. nitricum (3 mg. intravenously), especially in combination with strophantin (5 mg.) as recommended by Schiffner, occasionally yields a satisfactory result. As a general rule we do not administer cardiac tonics intravenously because just in those cases, in which a prompt effect is most desirable, this form of application is not entirely free of risk.

Quite often we make use of pituitrin in the form of subcutaneous or intravenous injections, first advocated by Klotz in cases of peritonitis. We repeatedly observed its invigorating effect on the heart and in our practice it now replaces adrenalin which we used to give. The latter we employ at present solely as addition to an intravenous saline transfusion or as a last resort measure in actual stoppage of heart action. In several instances we have observed excellent effect by direct injection of adrenalin into the left ventricle. Its subcutaneous injection in cases of evidently poor circulation seems risky since insufficient blood supply of the skin with the added local anemization caused by the extract necessarily increases the danger of local gangrene and of a secondary infection.

Adrenalin medication for peritonitis finds its theoretical justification in the fact, repeatedly confirmed by us in nec-



ropsies, that in cases of peritonitis, but never in a general sepsis without peritonitis, marked pathologic changes often can be discovered in the adrenals. These consist in a characteristic gray-reddish discoloration of the narrowed cortex, suggesting reduction of the lipoids and thus a functional exhaustion, of the adrenal system. This theoretical explanation of the usefulness of adrenalin, however, is somewhat weakened by our own observation that pituitrin proves not any less effective in these conditions.

### Saline Infusion

We use extensively the subcutaneous or intravenous saline infusion for the purpose of cardiac stimulation. To avoid any excessive strain we limit the quantity to 200 or 300 c.c., which might be repeatedly injected, but on principle prefer its administration in form of the rectal drop. In this form no limitation need be placed on the amount given. Its effect is limited to cardiac stimulation. We do not believe that saline solution, as seems the common view, actually "flushes the body and washes bacteria and toxins from the tissues."

Obviously we must meet certain arguments naturally to be raised against our point of view. How could this assumed disintoxication be achieved? If we look upon the puerperal process as a bacteremia it could be influenced beneficially only by the prompt elimination of large quantities of bacteria through the kidneys. I am thus forced to discuss briefly the problem of the elimination of bacteria in the urine.

Are bacteria weeded out only by the damaged kidney or can they pass also through healthy renal tissue? There are but two possibilities.

1. The bacteremia causes a nephritis, and renal damage leads to the bacteriuria; or
2. Bacteriuria occurs also in the presence of a clinically intact kidney.

In my belief the second possibility must be readily admitted. A bacteriuria is often seen in various of the acute infectious diseases, e.g., typhoid. The bacteriuria must be accepted simply as an excretory phenomenon though it might be increased by an incidental renal lesion. Studies at the postmortem table show that in most acute infections anatomic lesions can be discovered in the kidneys even in the absence of all clinical manifestations. They permit passage of the organisms through the walls of the glomeruli but it is not justifiable to look upon these lesions as specific tissue alterations enhancing the chances of recovery through free elimination of germs from the body.

These particular conditions years ago have been carefully studied in an experimental way (Jahn, Wyssokowitsch, Kraus and Biedl), although the results were not conclusive. While some found the intact kidney entirely impervious for spores or bacteria, and their passage strictly dependent upon marked pathologic changes, others claim to have observed their elimination as well by the healthy kidney.

I accept the latter view, chiefly because we know that during the functional test of a certainly normal kidney such corpuscular elements as particles of dyes readily pass through the organ. The relation between renal lesion and the passage of bacteria probably is best expressed in the formula, that the damaged kidney always allows large quantities of bacteria to pass, while in the healthy kidney their number in the urine is so small that they are easily overlooked.

Whether many or only a few organisms are eliminated by the kidneys certainly can be of no importance in the outcome of a puerperal infection, when thrombi or other foci again might throw enormous quantities of them into the system at any time. Nobody claims that the saline infusion could flush the bacteria out of these hiding places.



Still greater difficulty is experienced in justifying the use of saline, if one regards puerperal infection as a toxemia although, disregarding a streptococcus infection, this assumption is true at least in part for other types of infection.

In view of the known rapid and firm attachment of toxins to tissues (thinking, e.g., of the effect of the virus of tetanus or lyssa on neural tissue) it seems impossible to imagine that these associations between toxin and tissue can be easily dissolved and that an attenuation of the toxin concentration in the body fluids will be readily achieved by increased diuresis.

However, even granted a prompt reduction of toxins, such reduction can be of but limited value since new toxins are continually formed. In the septic puerpera we are not dealing with a definite quantity of poisonous substance like in the animal experiment with artificial infection in which dilution often means permanent reduction. It is the very characteristic of the septic process, especially of the hematogenic type, that new organisms intermittently or constantly enter the blood stream. With each new addition of germs and their disintegration we are dealing with a renewed exacerbation of the toxemia. It is unjustified to expect amelioration of the toxemic condition without simultaneously effected destruction of the germs at their source. "Every infection," writes Schottmueller, "is accompanied by intoxication. Their association is inevitable. To combat the latter we must eliminate the former."

From this point of view any belief in the disintoxicating effect of saline infusion is entirely problematic. Its effect is due to improved circulation owing to better filling of the vessels. Total anemization of the patient by undue accumulation of blood in the abdominal vessels is prevented. Decidedly more benefit can be derived from sugar solutions (5 to 10 per cent or even higher concentration) because they supply not only desirable nutritive material but also

stimulate the heart (Copeland). I shall refrain from considering their further value on account of their osmotic action as suggested by Stejskal, but it seems possible that in this sense also higher concentrated solutions of sodium chloride and other salts might prove of value.

### Cathartics

Those who advocate the use of cathartics in the treatment of puerperal fever (MacCann and others) explain their supposed efficacy on a principle rather similar to that assumed for saline infusion, namely, that they cause a free elimination of toxins through the bowels. We prefer to agree with the view of most clinicians that diarrhea can be regarded solely a weakening factor which must be ameliorated rather than aggravated. For this reason we prescribe an appropriate diet and give opium, or its derivatives (pantopon,<sup>4</sup> holopon,<sup>5</sup> etc.), tannin, bismuth, resorcin and other astringents.

For this same reason we reject enteroclysis (recommended by Hirsch). Forced sweating seems objectionable because the resulting concentration of the blood, owing to concomitant concentration also of its toxic contents, would more likely render the patient's condition worse.

B. O. Pribram ascribed the septic diarrhea to a reduction of acid and pepsin concentration and claimed good prophylactic and curative results for acidol-pepsin.<sup>6</sup>

### Alcohol

Much discussion has been aroused by the question of the possible value or actual disadvantage of alcohol in the

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<sup>4</sup>An opium extract which contains the alkaloids in the form of hydrochlorates. In effect, one unit of pantopon corresponds to five units of opium. It is a brownish powder, easily dissolved in water.

<sup>5</sup>It is an ultrafiltrate of opium, comprising all its active principles, containing 10 per cent of opium.

<sup>6</sup>Betain-hydrochlorate with pepsin. White crystals which, when dissolved in water, give off 24 per cent hydrochloric acid. This preparation is on the market in two strengths.

therapy of puerperal sepsis. It would be useless to enter here into the theoretical phase of the problem, especially since it is presented in detail by v. Herff in Winckel's *Handbuch der Geburtshuelfe*. V. Herff arrives at the conclusion that alcohol is just as superfluous for the febrile puerpera as it is for the healthy and well nourished individual. In this attitude he is supported by Opitz who considers any easily combustible substance (most of all cane and grape sugar) a perfect substitute for alcohol. V. Herff's views are shared by Binz, Martin and Kroenig. Also Monro and Findley deny to alcohol any medicinal value, consider it contraindicated in any case and readily replaced by many other drugs not less effective but certainly less dangerous. They do not believe that alcohol is a cardiac stimulant or possesses any antitoxic properties.

Among the defenders of alcohol we can mention Pinkham, Cragin (using it in combination with strychnine), v. Rosthorn (only in small doses), Galabin (large doses), MacCann, McIlwraith, Doederlein, Burthenshaw ("because it not only stimulates but also has nutritive value"), Lenhartz, Davis, Breisky, and Runge (medium doses).

Jungbluth found alcohol to be a satisfactory antipyretic in experiments on animals. He introduced into the stomachs in one-half of a series of infected dogs water, in the other half alcohol. Administration of alcohol was followed by lowering of temperature.

We acknowledge the wide discrepancy of views in this problem. However, as usually also here the middle course most likely will be the best, and it is the one we have adopted.

Small doses of alcohol can hardly yield any striking therapeutic effect and most assuredly will not exert any bactericidal power. It is not permissible to apply in this respect certain results, obtained in experiments *in vitro*, to the human being.

Large doses, employed for a short time only, may be free of harm but will hardly do much good.

We consider alcohol a beverage without any medicinal value, and fare well allowing it in medium doses to the patient who may need or desire it. Expensive sweet wines and champagne are not at our disposal for clinical use, but good white wine and claret serve fully our purpose of stimulating appetite and much more we do not expect.

Alcohol in concentrated form (rum, cognac, brandy or whiskey) added to a hot drink like tea or lemonade is of some advantage as a restorative immediately after a chill. As already stated we have no definite rule for the use of alcohol, and in the main are led by the patient's own desires.

### **Application of Heat**

Heat applied by means of a hot water bottle, electric pad or electric light arch is of value during a chill and hastens the resorption of an exudate, but the heat of such appliances never suffices to actually kill bacteria.

### **Roentgenization**

Encouraged by good results obtained in the treatment of tuberculosis, roentgenization has been recommended for the treatment of puerperal infections by Doederlein, and Jakobs. Large doses of hard rays applied two or three days in succession apparently had a most satisfactory effect.

We had the same thought and had tried the rays in one or two cases some time ago, but noticed no benefit from them. We were led by the experience that x-rays must have a bactericidal effect since cultures exposed to them show distinct retardation of growth and so we expected a similar favorable effect for our patients. We furthermore hoped that radiation of the bone marrow and of the spleen

might stimulate leucocytogenesis. Not having continued these experiments we are unable to pass judgment, but Laewen's findings certainly contradict our assumption. He observed that exposure to x-rays reduces the resistance of animals against bacterial infections.

It would seem possible that good effects recorded with the quartz and uviol lamps or "artificial sun" in some infections (tuberculosis) could be duplicated in puerperal fever cases. It might be worth the while to test such appliances on a large material.

Unfortunately these various methods cannot be made available to the many patients sick in their own homes, and their transport to hospitals for this purpose would conflict with one essential feature of their treatment, namely undisturbed rest. Of course, this disadvantage would be more than outweighed in case the efficacy of these curative methods was firmly established.



## CHAPTER IV

### LOCAL THERAPY

The field of local therapy is rather narrow, being restricted practically to only two tasks: (1) to cure pathologic local manifestations, which often can be accomplished easily, and (2) its chief purpose, to prevent a systemic infection from the primary focus, a problem of greater difficulty and often impossible to solve.

One might say of all these efforts especially in the latter respect that they are characterized by their multiplicity rather than by their utility. A certain meddlesomeness along these lines is evident in modern therapy. While this holds true particularly for French, English and American obstetricians, the majority of German accoucheurs take a markedly negative attitude.

At least from a theoretical point of view it seems surprising that in spite of the many good antiseptics at our disposal we experience such difficulty in mastering a localized infection even if comparatively easy of access. Most of these antiseptics kill quickly even germs of high virulence—in the test tube. I have already had occasion to emphasize this obvious difference between the experiment *in vitro* and the actual experience on a patient.

Disregarding possible variations in virulence and growth, in the experiment *in vitro* we naturally ignore the incidental destructive effect of an antiseptic in higher concentration on the culture medium. Dealing with the same problem in a human being, we are forced to recognize the fact that the germ usually proves more resistant to the disinfectant than the host, to say nothing of the possible general toxic effect of the antiseptic. The other great difficulty, though



not important just in the most common and most dangerous streptococcic infection, is that it becomes necessary not only to destroy the bacteria, but also to rid the body of certain toxic substances produced either by them or through tissue changes resulting from the infection. Our therapeutic failures are due to the multiplicity of the problems presenting themselves in the individual case and to the definite limitations in the application of powerful antiseptics.

### **Treatment of Perineal Ulcerations**

The therapy of these ulcerations in general is simple enough. Dirty ulcers are treated with caustics. If necessary, remaining sutures are removed and the wound laid open for better drainage. The most useful antiseptics are: tincture of iodine and iodoform, the latter applied as powder or in form of a salve; carbolic acid in solutions between 10 and 20 per cent, or concentrated. Some authors prefer salves, especially those containing boric acid. Byers adds one gr. of anophen to 6 gr. of boric acid salve. The cleaning of the wound with a watery or alcoholic solution of bichloride or formalin, varying in concentration, proves of great use.

Not so marked in their immediate effect but serviceable for superficial processes are solutions of lysol, lysoform, carbolic acid, cresol, and the halogens: iodine, bromine and chlorine. Of late much benefit is claimed, especially in infections with anaerobes, for the Dakin solution.

Dupont recommended the treatment of puerperal ulcers with hot air, obtaining thereby not only bactericidal effect, but also a hyperemia of the tissues. He first cauterizes the sores with air of 80 to 90° C. sufficient to destroy the bacteria, and then blows for five to ten minutes warm air of 50 to 60° over the ulcers.

The suggestion of inoculating the lactic acid bacillus on these ulcers came from French authors. A bouillon cul-

ture mixed with a sufficient amount of milk sugar to form a paste is applied. The effect is supposedly a double one, antiseptic through the lactic acid, and chemotactic through the sugar. In general the procedure concurs with the assumed effect of the lactic acid douche of Zweifel and Schweitzer mentioned in foregoing pages. Both methods are based on the fact that the streptococcus grows very poorly on an acid medium. The lactic acid bacillus is not pathogenic for man and indeed is more or less physiologic as far as the female vagina is concerned.

We have found that daily painting of the ulcers with tincture of iodine and washing of the external genitalia with an antiseptic solution (potassium permanganate in our routine) is so satisfactory in its results that all the more complicated procedures can be dispensed with.

Decidedly more obstinate one will find ulcerations situated higher up in the vagina. Complex manipulations, use of speculum, etc., are unavoidable, especially because such lesions drain poorly, heal more slowly and thus increase the risk of a systemic infection. Made visible in a speculum they are treated with caustics like the perineal ulcers.

### Vaginal Douches

The vaginal douche, as commonly used, has as little curative value as it has prophylactic. We have already mentioned the reasons for this failure. Whatever effect it actually has lasts but a short while; the marked absorbent faculty of the vagina prohibits the employment of most antiseptics in higher concentrations.

Long continued irrigation probably yields better results, not through its disinfectant qualities, but alone by reducing germ concentration through continuous mechanical removal of vaginal secretions. Potassium permanganate for this purpose offers the great advantage of not being

a poison but an effective deodorant and incidentally also particularly destructive for anaerobes. Obviously as well other solutions can be used, e.g., lysol, cresol, formaldehyde, etc.

We order the vaginal douche only in the presence of a profuse fluor, especially if the odor is offensive, and then simply as a symptomatic remedy, but we do not look for any specific or curative result from its use.

Hornstein claims to have treated most effectively septic colpitis or vulvitis with a 10 to 20 per cent emulsion of calcium hyperoxidatum or with this substance in powdered form, pure or mixed with talcum (1:5). Its symptomatic effect seems natural, but it probably is not any more valuable than any other mixture of powders.

### Uterine Therapeutics

Opinions are divided concerning the attitude to be taken in regard to an infected uterus or one suspected of being infected. The multitude of measures that have been proposed in this respect, of themselves prove that we do not know of a single one that is thoroughly satisfactory. The main questions are these: Should one attempt to completely remove, or at least to render innocuous, the primary source of infection within the uterus? Or is it preferable to let the contaminated uterine cavity severely alone, because any manipulation within it is apt to foster the one thing we must try to avoid, namely, a propagation of the septic process into the general system?

First of all it is necessary to differentiate sharply between the uterus postpartum and the uterus postabortum. Towards the latter at least German obstetricians exhibit no excessive fear, while with but few exceptions their attitude regarding the uterus postpartum is extremely conservative.

**Uterine Douches.**—The comparatively simple procedure of uterine douche is considered by many writers as very valuable. They recommend various antiseptics for these douches and describe various instruments and apparatus for their administration. As a whole all I have said about vaginal douches probably holds true as well for uterine douches.

More than a temporary effect cannot be looked for. In view of the markedly greater absorbent power of the endometrium as compared with the vaginal lining, we have to be still more careful in the selection of the antiseptic. Therefore again we can count only on a certain mechanical effect but not on any bactericidal action of the fluid flushed through the uterine cavity.

As compared with the vaginal douche, uterine lavage brings the added danger that it might actually force micro-organisms into deeper layers or into open lymph channels because the inner surface of the puerperal uterus never is intact. These inevitable wounds and injuries, in case of extreme softness of the myometrium, might have penetrated the wall and then the antiseptic fluid really is washed directly into the peritoneal cavity.

I remember a case in which we made use of the uterine alcohol douche, at that time enjoying much favor. During its application the patient died within a few minutes. The very experienced attending physician had observed that the fluid suddenly had begun to flow faster from the receptacle. Autopsy showed a uterine perforation but no peritonitis. The patient had succumbed to a very acute alcohol intoxication.

Quite recently I had occasion to make a similar observation. On the fourteenth day postpartum a febrile patient was given, in her home, 2000 c.c. of a 25 per cent solution of alcohol as uterine douche. During the procedure she became unconscious. When admitted to our clinic she was in a stupor, cyanotic, breathing stertorously, pulse hardly palpable, pupils wide and reactionless. Camphor was injected, as well as caffein and strychnine. Finally a saline infusion with some adrenalin improved cardiac action, but with cessation of infusion she im-



mediately grew worse. Exitus a few hours later. Necropsy revealed no perforation but diffuse peritonitis and thrombophlebitis.

Such unfortunate sequelae possibly are not common, but one must keep in mind that a therapeutic procedure is truly useful only when its application is not limited to the well-equipped hospital, but is readily available in general practice without any demand for particular skill and dexterity required for its execution.

Occasional failure and even occasional harm can be disregarded in a therapeutic method that is characterized by good results, but this cannot be said of the uterine douche. Therefore the possible damage must be accepted as a serious warning against its use.

Another element of risk is the possible flushing of the antiseptic solution through the tubes into the abdominal cavity. This might be obviated with very low pressure by holding the douche-can not more than 50 to 100 cm. above the level of the douche-point. That this danger, however, is not always successfully eliminated is shown in the second of the two cases just described.

Not all writers share our views in regard to the uselessness and dangers of uterine douches. They are recommended by many French, American and English obstetricians and among Germans I might mention Doederlein or Weil. Usually the advocates recognize definite indications and contraindications. French writers consider uterine douching justified only within the first few days when the infection still is limited to the uterus, but warn against it after the eighth day when the process likely has reached surrounding tissues. Most favored are normal saline solution, alcohol in varying concentration, iodine, lysoform,<sup>1</sup> bichloride, etc., of late Dakin solution (Trillart, Hellendal, Whitehouse, and Anderoidas). The last mentioned author

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<sup>1</sup>It is a yellowish, odorless fluid, containing formaldehyde and spiritus saponis which does not harm skin, instruments or linen. It is less poisonous than lysol but probably also less bactericidal.



introduces a catheter into the uterus, connected with a bottle containing the solution, fastened about 75 cm. above the level of the bed. Every two or three hours from 40 to 50 c.c. of the fluid are permitted to flow into the uterus. The procedure is continued for eight days. The vagina is protected by a gauze packing soaked in vaseline.

Merely as a curiosity I mention the very complex procedure of Sitsinsky. By employing in repeated douches bichloride, boric acid and alcohol he expected not only to keep the uterine cavity dry but "to create a reversion of the molecular stream into a direction opposed to resorption."

A middle position is held by Arnold, Schlueter, and Keller who would like to see the uterine douche used less often than at present is the case.

As opposing the douche we can mention Clement, Toff, Zweifel, Perrenaud, King and others, who are afraid of the bichloride intoxication, of the entrance of air into open veins, or of escape of the fluid through the tubes into the abdomen, all these being valid arguments against the utility of the procedure. Particularly dangerous in regard to possible air embolism are hydrogen peroxide and other gas-forming chemicals.

**Introduction of Steam or Gas into the Uterus.**—This last mentioned danger as well is inherent to the persufflation of the uterus with oxygen as advocated by Thiriar and Reverdin, and considered particularly valuable in cases of anaerobic infection by Reynier. While in principle apparently correct such procedures in practice are too risky. One might assume that at the time of application all veins had been closed up by thrombi, but the dislodgment of such a thrombus might open a vessel for the entrance of gas.

More extensive observation alone will show whether Warnekros' method of introduction of ether vapor into the infected uterine cavity can do all that is promised for it.

Personally I doubt that the bactericidal power of ether is sufficient, or that even achieved sterilization of the uterine cavity would greatly influence the further course since in all likelihood at that stage the infectious process has already invaded adjoining structures.

It appears that so far definite indications for the use of these various flushing procedures have not been determined. Pedraja, e.g., claims good result from them "as long as the infection is limited to the endometrium," and Pinard and his pupils refuse to employ them after the eighth day "because at that time the infection not any longer is confined to the uterus." In practice such statements offer no guidance for action because, as a matter of fact, we do not possess any signs or findings which definitely indicate whether the process is still strictly localized or has spread to neighboring tissues. Cases of rapid spread, in which the infection affects adjoining tissues within a few hours, are not rare and thus the limitation to eight days, as proposed by Pinard, is deprived of all justification. Has the infection transgressed the limits of the uterus, then the various inevitable manipulations especially, such as pulling the cervix downward, tend to do enough harm to outweigh any possible advantage.

I have already spoken of the complexity of Sitsinsky's method and of the drawbacks of the use of alcohol and bichloride on account of their toxicity. One may well doubt Sitsinsky's assertion that his procedure preserves the protective wall of granulation tissue and never injures the treated surfaces, that the alcohol completely exsiccates the uterine cavity and that he is able to reverse molecular motion.

Some effect, though probably not great, might be expected from often repeated flushings and more particularly from the continuous douche which prolongates the germ-reducing ability of the douche. But again, all this implies

more manipulation and thus more chance of having possible benefit counteracted by incident harm. Therefore it seems inadvisable to recommend any of these various forms of intrauterine procedures for curative purposes. They are restrictedly useful immediately before operation in spite of the short duration of the disinfectant effect. For their application we find the usual double-barreled uterine catheter in its various models just as practicable as any of the complex apparatus which has been described. The essential principle in applying a uterine douche is the necessity for unobstructed outflow of the fluid or gas introduced into the uterus to prevent leaking through the tubes into the peritoneal cavity.

**Removal of Placental Rests from the Uterus.**—Uncomparably more fertile than the question of intrauterine douching has proved the problem of curettage of the puerperal uterus for useless and contradictory discussion in medical literature. It appears that as a whole the German writers take a more conservative attitude, while some of the foreign schools seem extremely radical. The divergence of opinions often borders on the grotesque.

Even those in favor of active interference dissent on the procedure best suited for evacuation. One group favors digital removal of the remnants, the other repudiates anything which is not accomplished by means of instruments. Some writers are satisfied with the mere removal of the remaining tissues, others insist upon subsequent douche, chemical cauterization, packing, etc., or even propose to utilize the wounds set by the operation for the quicker resorption of certain antiseptic agents which are supposed to heal the local or systemic infection.

The present status of the problem is best shown by citation of some of the views held by various authors.

Pinard and his pupils, Daniel, Rasis, Charles, Hubart, Lepage, etc., enthusiastically recommend the curette,

though with a few restrictions: it should be used only after a preceding trial with a uterine douche has failed, and should not be employed either before the third or after the seventh day.

Demelin, Buman, Noble, Cragin, McIlwraith and others favor digital evacuation, possibly with subsequent drainage. French obstetricians, after the removal of the retained tissues with the finger, often clean the uterine cavity with a stiff brush (*ecouvillonnage*). Potvin designed an instrument (*pince a faux germes*) which has the advantage over the curette in that it does not injure the protective wall of leucocytes.

Judging from literature it seems that French authorities are disinclined to differentiate whether curettage is done in a uterus after full term labor or after abortion, and whether this uterus is infected or not. Very similarly proceeded some of the American and English obstetricians who, disregarding a possible infection and still more the type of the pathogenic organism, advocated curettage even if the retention of portions of the placenta is only suspected (Vineberg, Wilson, Whitehouse), or insist on digital removal of smaller or larger pieces of placenta (Blair Bell, Fisher, Holladay, Safford, Miller). A decidedly more conservative attitude has become apparent only of late and at present most of the standard American textbooks of obstetrics and gynecology warn against curettage of the infected uterus. As late as 1913, Pinkham insisted that in the treatment of a septic abortion only the sharp curette should be employed, because only with it is it possible to remove the entire mucosa sheltering the streptococci.

Those still favoring active interference now are outnumbered by those preaching conservatism, especially as far as curettage of the infected, full term uterus is concerned. Many authors insist that instrumental evacuation of the uterus is permissible only under certain conditions—when



the life of the patient is in immediate danger (Jackson, McCann, Watson). The tendency towards noninterference is noticeable now also in French literature. Vignes, e.g., is against curettage, curage (digital removal of uterine contents), or application of strong antiseptics to the infected endometrium, and he considers intrauterine douches useless. He thus comes markedly nearer to views propagated for some time now by German writers, by Opitz, v. Rosthorn, Queissner, and most of all, by Winter and his pupils.

It is generally known that Winter, in the presence of the hemolytic streptococcus, also for cases of abortion considers any intrauterine interference justified solely if the patient's life is endangered by a severe hemorrhage, but otherwise treats all cases expectantly. Various publications and discussions show that the followers of Bumm (Runge) occasionally advocate digital removal of the remaining placental tissue, Lenhartz restricting this procedure to abortions within the first three months.

We deal conservatively, without any exceptions, with the uterus postpartum and on principle refrain from any instrumentation in the presence of a puerperal infection exempting from this routine alone cases in which an excessive hemorrhage, caused by placental rests, could not be controlled by tight packing of the uterus. This teaching is based on our conviction that every intrauterine procedure can do harm. Many experiences have convinced us of the justification of this attitude and only increased the rigidity with which we have adhered to this principle as far as the full term uterus is concerned.

It can be admitted that a careful digital exploration will not open new wounds, but certainly the removal of adherent coagula and fibrin creates new areas from which resorption will take place; thrombi will inevitably be torn loose and thus new gates opened for the entrance of pathogenic germs into the blood stream. Even with extreme



caution the exploring fingers necessarily force bacteria into the blood, as well proved by the chill commonly following the cureage. And then we never know whether this one chill is solely the immediate consequence of the procedure or possibly the starting point of a series of chills, unquestionably due to our actions. I might mention here, that Bonnaire claims to have prevented the subsequent chill by thorough painting of the uterine cavity with an extra strong tincture of iodine, one or two hours before the contemplated operation. Our attitude concerning intrauterine treatment obviously has prevented us from testing this suggestion but theoretically it seems not to possess much value.

Our apprehension in regard to all intrauterine interference postpartum is mainly caused by the fear of propagating the extension of the infection into tubes and to the peritoneum through inevitable motions of the uterus. One never knows whether these structure are still intact and manipulations of the uterus necessarily will endanger them, since only absolute rest will cause the puerperal process to halt or to regress.

Afraid even of digital evacuation we cannot find the courage to resort to curettage of the puerperal uterus. All we have said concerning cureage with still greater force applies to curettage. Without fail new wounds are set not only in the mucosa but also in the myometrium. Many blood and lymph channels are torn open, with even greater pressure pathogenic germs are directly pushed into circulation. The cervix must be caught with a volsellum and the uterus pulled down. For these reasons we repudiate the doctrines of the activists, in spite of their attempts to reduce inherent dangers by certain details of technic.

Champetier de Ribes insists that curettage must be done "before the bacteria have penetrated too deeply and have gotten out of reach of the curette." We doubt that even

the most experienced man can estimate the degree of existing penetration from the clinical picture or can in this respect depend upon the duration of the process. Pinard's school definitely limits curettage to the first eight days "because later the infection is no longer localized in the uterus." I feel that such limitations are arbitrary. How long the process will remain confined to the uterus is chiefly determined by the virulence of the germs and their peculiar tendency to invade tissues, however, to a marked degree it also depends upon the patient's resistance. Everybody has seen severe systemic infection three days, two days, and possibly on the first day postpartum and, on the other hand, has had occasion to observe cases in which a puerperal infection even after weeks still remained restricted to the endometrium.

Neither indication nor justification for curettage can ever be found in the duration of the process. The operation might seem permissible solely on the basis of certain clinical features of the individual case.

One can appreciate the endeavor of Champetier de Ribes or of Pinkham to rid the uterus of these harmful bacteria, but we disagree on the direction in which they will leave the uterine cavity after the use of the curette.

There might be justifiable disagreement concerning the protective faculties of the layer of granulation tissue, but it seems reasonable that it will offer some sort of obstacle to germs of low penetrating ability, and therefore its destruction cannot be without some significance for the further course of the disease. We maintain, against the opinion of Gordon, that this leucocytic defense should be respected, which is impossible when making use of the curette.

Once more and with emphasis I will state that our conviction of the advantage of a thoroughly expectant attitude pertains alone to the infection of the uterus postpartum.

We are decidedly more active in dealing with uterine infections after abortions within the first three months of pregnancy. In these cases we empty the uterus and most often with instruments. We accept as the one strict contraindication an affection of adjoining structures, but entirely disregard the type of germ, even the *Streptococcus hemolyticus*, without ever having seen any harm come from a practice which is so little in accord with the teaching of Winter and the Koenigsberg school. As shown in detail in the paper of Patek, presenting the results of our clinic, we have adopted this practice for various valid reasons. The dull curette removes placental rests with less traumatism to the uterus than the finger. Determination of the germ type responsible for the infection before interference from a theoretical point of view is ideal, but in practice applicable only to those comparatively few abortion cases which fortunately are managed in a well-equipped hospital. Uniformly satisfactory results have induced us to continue this routine as more recently set forth by our chief, Professor Halban.

Speaking again of the puerperal uterus, our conservative standpoint offers us no opportunity to make use of such therapeutic measures as painting its cavity, packing, draining or producing an artificial hyperemia by suction. However, for the sake of completeness I shall discuss these procedures.

**Swabbing, Packing, etc., of the Uterus.**—Applications of strong antiseptics to the uterine lining are assumed to destroy or reduce the bacteria present. The introduction of but a small quantity of fluid in this manner is considered an advantage over the intrauterine douche. Often a more lasting effect is supposed to be obtained by packing into the uterus a gauze strip soaked in the antiseptic. Various drugs have been recommended for this purpose: tincture of iodine, iodine (in a 0.4 per cent solution in distilled

water), carbolic acid, dermatol,<sup>2</sup> iodoform, and more recently yatren.<sup>3</sup> In use, the last mentioned powders probably prove more practical because they are readily available, while strips soaked in a solution require preparation at the time when they are needed.

A certain popularity seems to be enjoyed by gauze wet with alcohol (Carossa), with hydrogen peroxide (Budin), or with turpentine (Delmas and Fabre). Turpentine resorbed into the system from the uterus is assumed to stimulate incidentally also the leucocytes.

Clement applies first tincture of iodine and then introduces a gauze strip soaked in horse serum, which previously had been heated to 56° C. (after Petit). This preliminary procedure, in his opinion, prevents the usual chill subsequent to a required excochleation. If the fever continues he repeats the entire procedure after twenty-four hours.

Sinclair prefers gauze moistened in bichloride, Doleris, in a mixture of creosote and glycerin, while some American writers seem to favor a formalin solution.

Since all these procedures require manipulations of the puerperal uterus and endanger the protective wall of granulation tissue, we class them with all the other intrauterine measures and doubt their beneficial effect. The introduction of gauze strips for the purpose of a prolonged disinfectant effect will necessarily lead to a retention of secretion and again we fear that resulting increased resorption will more than outweigh the benefit of the achieved destruction of a few more germs.

**Drainage.**—Effectual drainage certainly would preclude any possible accumulation of noxious secretions and therefore its recommendation by many authors is easily understood. Unfortunately, however, the difficulties of obtaining

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<sup>2</sup>Bismuthum subgallicum, a yellow, tasteless and odorless powder, not soluble in water. Occasionally it causes erythema, possibly also the symptoms of bismuth poisoning.

<sup>3</sup>Iodoxychinolinsulphonic acid, containing 25 per cent of iodine. This preparation is further discussed in the text of a later chapter.



such drainage are great. I shall discuss the various methods of drainage in detail in a later chapter dealing with the therapy of peritonitis.

Very generally either gauze strips or tubes, made of rubber, glass or metal, are employed. As already stated, gauze strips are more apt to obstruct than to favor the escape of the usually thick and tenacious uterine secretions. Rubber drains often fail to serve their purpose by becoming kinked or compressed. Therefore glass or metal drains as a whole are more useful, but when retained for a long time they tend to cause decubitus.

Henckel described a special glass tube filled with a replaceable gauze wick soaked in quinine-alcohol. Similar is Dowd's procedure. He introduces a rubber tube, filled with iodoform gauze, up to the fundus and packs the uterine cavity loosely, but the vagina firmly, with iodoform gauze. Through the rubber tube, every two hours, about 50 to 60 c.c. of 25 to 50 per cent alcohol are permitted to flow into the uterus. This method is claimed to have a marked disinfectant effect, causing the temperature to sink, as a rule, after 16 hours. Of 105 patients treated in this manner 85 recovered. Fraenkel recommends the prolonged drainage of Hegar with repeated flushing with a chlorine solution (100 to 250 c.c. of chlorine-water to 1000 c.c. of fluid).

Wetherill flushes the uterus repeatedly through a double catheter with 60 to 100 c.c. of a 50 to 60 per cent solution of alcohol. The method of Anderoidas I have already mentioned.

From this selection of suggested procedures it might be seen that their advocates seem to depend rather on the effect of flushing but try to avoid the necessity of repeated introduction of an applicator or of a douche-point.

Mentioned solely to be condemned is the proposition of Chandler. He opens the posterior culdesac and with a



uterine forceps makes three perforations through the uterine wall to introduce gauze strips into the infected uterine cavity, their free ends hanging through the posterior fornix into the vagina. The risks inherent to such a procedure are too self-evident to require discussion.

In my opinion drainage can be desirable only in the relatively rare instances of a lochiometra. It will become superfluous in most cases because the retention of foreign tissues within the uterus as a rule causes the cervix to remain gaping. For the expulsion of stagnating secretions under these conditions the force of the contracting uterus should prove sufficient, especially if contractions are stimulated by proper medication.

**Suction Treatment, Artificial Hyperemia.**—In view of the evident shortcomings of all methods of drainage, it is but natural that efforts have been made to hasten evacuation of the uterine cavity by suction in spite of the obvious inaptitude of the organ for such a procedure. According to physical law a fluid can be effectively sucked up only if the end of the suction tube dips into the fluid. This is impossible in the case of the puerperal uterus with the sole exception of an actual lochiometra, because in general here the problem consists in the removal of a sparse discharge and therefore, only so much of it will be drawn out as accidentally comes in contact with the end of the tube. This is hardly enough to justify the use of so complicated an apparatus. Aspiration really results in nothing more than in the hyperemia which Bier attempted to produce, and as a matter of fact this idea of sucking out the uterine secretions was introduced into obstetric therapeutics at a time when every branch of medicine attempted to make use of Bier's hyperemia therapy.

Seeligmann, Kroemer, or Sitzenfrey claimed good results for this method, the latter reporting five cures out of seven

cases in which he employed an apparatus specially designed by him for the purpose.

Somewhat different and more complex is a technic suggested by Queissner. He endeavors to kink uterine blood and lymph vessels by elastic traction on the cervix. In this manner he expected to obtain not only a passive hyperemia, but also to hinder the transition of toxins from the primary focus of infection into the general system. It seems extremely doubtful to me that this latter result could be achieved by this procedure.

In this same group of therapeutic methods belong furthermore applications of heat and of hot air. They also are based primarily on the resulting hyperemia and only secondarily on a possible disinfectant power of very high temperatures. The hyperemia might well be secured, but even the introduction of overheated steam (atmocausis of Pinkus) destroys only those bacteria immediately exposed to it and certainly not those lying well sheltered in closed folds or distant corners. The steam-cooked surface layers, which form immediately, in my opinion, actually protect organisms situated a little deeper against any possible damage from the steam which continues to flow into the uterus.

As in so many other efforts to kill bacteria, here also we are facing the fact that bacteria often prove more resistant than the surrounding living tissues and bactericidal efforts too energetically pushed might inflict irreparable harm on the patient.

The cooked necrotic tissue, one must not forget, finally provides a splendid medium for further bacterial growth, thus probably in the end annihilating the primary good effect of steaming. We, therefore, cannot recommend the atmocausis of Pinkus for the treatment of the infected uterus.

Another procedure, likewise based on the principle of destroying bacteria by excessive heat, consists in placing

the patient in a very hot bath or into a hot air apparatus. Good results have been claimed for the method especially in the treatment of gonorrheal infections; it has been but rarely tried for puerperal sepsis. Outside of other objections the one most valid would seem that this heroic procedure inevitably places a considerable strain on the heart, a factor not to be disregarded in a chronic septic individual. Not even diathermy raises body temperature to such a degree that bacteria, and especially streptococci, would suffer serious damage. Gonococci, known to be decidedly less resistant to heat, in many observations have been found to remain unharmed, and in contrast to a few years ago one reads but little of this method in recent literature.

The relative inaptitude of the measures just discussed in the therapy of puerperal fever, however, does not mean that we must dispense with all forms of heat application. They influence local inflammatory processes beneficially by causing hyperemia and they afford to the patient much comfort through relief of pain. It seems irrelevant whether one uses for this purpose the electric light arch, electric pad, hot water bottle, hot air apparatus, hot moist packs or the time-honored poultice.

## CHAPTER V

### SURGICAL THERAPY

In connection with surgical therapy of puerperal infection in the main only three major operations have to be considered: (1) hysterectomy; (2) laparotomy for peritonitis, and (3) ligation of veins for cases of the hematogenic type of puerperal sepsis. Outside of these we have among operations of minor seriousness the incisions with subsequent drainage, most often made through the posterior fornix.

I shall discuss this large and complex problem rather briefly because it has been thoroughly covered in the exhaustive papers of Wormser and Venus and because nothing of sufficient weight has been published since that time to induce us to change our point of view in this matter.

One principle applies to all forms of operative interference in puerperal infections: They will yield satisfactory results only if they can be performed early enough and without any additional harm to the patient. These terse requirements incidentally also express the wealth of difficulties which often prevent a realization of the hoped for good effect. The decision of "early enough and not too late," which in practice often comes to mean the equivalent for "unnecessary" in individual cases, proves one of embarrassing perplexity. We do not know as yet which the clear cut indications for operation are, at least not as far as hysterectomy and ligation of veins are concerned. In regard to peritonitis the situation is better understood and nevertheless conditions are not more favorable.

### Hysterectomy

The present status of views concerning indication, technique and prognosis of hysterectomy as expressed in literature may be summarized as follows:

The first successful hysterectomy for puerperal sepsis was performed by B. S. Schultze in Jena in 1886. At once taken up by American surgeons the operation soon afterwards found many advocates also in Europe, especially in France. However, many antagonists as well arose. At the end of the last century much was written in favor of the method in Germany, while it was practiced in Austria but by only a few outside of Latzko. The situation gradually became clearer through exhaustive discussions before the congresses at Rome (1902), Madrid (1903) and Strassburg (1909). Still the divergence of opinions remains marked enough to justify their short consideration in this connection since no attempt has been made in the past few years to give an account of present results.

No definite answers have been furnished to the obvious questions: In which cases shall the uterus be removed? Which is the most favorable time? How shall it be done?—and most important: When is it better not to attempt the operation?

Even if certain indications for operations under certain conditions would be agreed upon, we should have to determine in each individual case at the time of contemplated interference, whether these conditions justifying an operation have already appeared, or are still prevailing. For this reason alone it is impossible to formulate an exact answer to any of the questions.

With the very first question of the general suitability of cases for hysterectomy we meet the dilemma: Should this operation be limited to infections still localized within the uterus and its adjoining organs, or can systemic infection be disregarded?



Arguments can readily be found for or against either attitude.

Theoretically, it is reasonable to assume that the complete removal of the primary source of infection necessarily will prevent a further spread of the disease into the patient's body. Practice contradicts this theory. As early as 1896, Halban demonstrated that amputation of an artificially infected extremity does not protect the animal against general sepsis. In similar experiments made by Zangemeister it was shown that amputation of the infected tails of mice saved these animals only if simultaneously antistreptococcus serum was injected. Conditions in this respect are incomparably more unfavorable so far as the infected uterus is concerned, an organ so intimately connected with the rest of the body through so many blood and lymph channels. (I shall later have an opportunity to speak of our own views on serum therapy). In practice it is well-nigh impossible to say whether or not the infectious material has found entrance into these blood or lymph channels. If it has, the operation is illusory. The decision cannot be made either from the character of the lochia or from palpatory findings. Even one negative blood culture is of little value. It only proves that at the time no microorganisms could be obtained from the blood stream. None might have been in it, or extremely few, so few indeed that they had momentarily been destroyed by the bactericidal ability of body fluids, or damaged to an extent that they could not grow on the particular culture medium. These all are conditions which might change within a very short time. Again, one positive blood culture does not permit the diagnosis of a systemic infection because it might be the accidental result of but one bacterial invasion which will not necessarily recur. For obvious reasons palpation will reveal the spread of the infection only if it has resulted in an infiltration of connective tissue.

All this leaves too much to the subjective judgment and personal equation of the operator to permit the formulation of exact and binding rules for interference.

Is systemic infection a definite contraindication? *A priori* one would have to answer in the affirmative, because a hysterectomy performed at that time would appear to be too late. Quite naturally arises the counter argument, that the removal of the harmful primary focus and the prevention of any further influx of infectious material, must enhance the chances of the body to rid itself of the bacteria which already have entered. Both views are being defended.

Strict limitation of the process has been demanded as indication for hysterectomy by Stone, Ferguson, Galland, Vineberg and Jewett, the latter observing that the results of hysterectomy are the best when performed "after the infection has passed its most virulent stage." Many other writers, among whom I shall mention Veit, Wormser, Compston, Daniel and Ricou, Pinard, Cragin, Coque, Findley, Watson, Oldfield, and Boldt, accept as justifying the operation only such conditions as: impossibility of removing adherent rests of placenta, perforation of uterine wall, uterine abscess or gangrene, or necrotic myoma.

The defenders of the other viewpoint exclude from hysterectomy only cases of fulminant sepsis. Cortiguera looks neither on sepsis nor peritonitis as a contraindication as long as it is proved that the uterus actually is responsible for the sepsis, and liver and kidneys are found to be intact.

Many French gynecologists seem still to follow the rules of Faure: The uterus shall be removed if curettage has not brought noticeable improvement within twenty-four hours, if neither temperature nor pulse rate are reduced and chills continue (Catinal). Similar views are held by

Wilson who, however, delays hysterectomy until the end of the second week.

Sippel maintains that bacterial toxins may exert so deleterious an effect that the removal of their source is inevitable. It is not necessary to proceed with the operation after the second chill, as has been proposed, but only when the life of the patient seems in danger. Pankow claims that failure is met with solely when the operation has been unduly delayed. A rather peculiar attitude is taken by Schickele who considers hysterectomy unjustified for many of these cases, because it is not necessarily the uterus that represents the source of further danger. The bacteria might have passed through the uterine wall without setting up an infection in the organ itself. Its removal then certainly is superfluous.

Those in favor of definite restrictions in regard to hysterectomy proclaim as contraindications: general sepsis, diffuse peritonitis, extended thrombophlebitis, marasmus, collapse, streptococci in the blood stream, metastases in vital organs (including the eye), leucopenia or a steadily diminishing leucocytosis, both indicating acute sepsis.

Far from solution is the perplexing problem of early operation versus waiting for a vital indication. Often a comparison is made with appendicitis, and it has been suggested to apply the principles now generally accepted in dealing with the acute appendix also to the puerperal uterus. This is hardly justifiable. An appendectomy on a relatively healthy or acutely sick patient certainly represents an operation of infinitely less risk than a hysterectomy on a debilitated septic puerpera. As a rule we will remove the appendix from a but little affected region, the uterus more likely from an infected pelvic cavity.

Nevertheless early hysterectomy has found its many advocates especially among French gynecologists. Latzko in Vienna performs the operation in every case, in which

for forty-eight hours the temperature remains between 39° and 40° C., or no improvement in other respects can be seen. Pankow, as already mentioned, ascribes every failure of hysterectomy to delay, though he was successful in two cases, operating as late as sixty-seven and forty-eight hours, respectively. Kroenig also saw two patients, operated on the third day, recover, while five patients, operated after the fifth day, died. I might repeat, Sippel waits for a vital indication before operating.

The chief argument against early operation is the fact that it unavoidably implies the extirpation of a very important organ that possibly might have been preserved without harm to the patient. In judging assumed benefit of operation one should ever keep in mind that *post hoc* certainly does not mean *propter hoc* in puerperal fever, a disease characterized by its uncertain prognosis.

Against Sippel's insistence to wait with the operation until a vital indication for the same is manifest, the valid objection must be raised that this really implies the delay of this serious interference until a time when the patient represents a decidedly bad operative risk.

If one actually believes in the value of hysterectomy, he must resort to this operation relatively early, as long as the patient's strength is still preserved and at least the probability remains of restoring her to health.

Various types of operations have been performed. Pankow, Koblanck, Kroemer, Deaver, Guiccardi and others prefer the abdominal route. Bumm, v. Herff, Sippel, etc., make a supravaginal amputation under certain conditions, while Boldt, Vineberg and Hirst resect only the diseased portion of the uterine wall. Others, like v. Rosthorn, Fehling, Daniel and Ricou, Galland, Maurique, Catinal, Potvin, give preference to the vaginal route, while Koblanck does a vaginal hysterectomy as long as the infection is limited



to the uterus, but a laparotomy when the process has advanced.

The following details of technic are noteworthy: v. Herff endeavors to destroy bacteria deeper in the tissues by burning all stumps with an electrocautery. Supravaginal amputation, in his opinion, means for the patient less risk and less chance of subsequent peritonitis as compared with total hysterectomy. Bumm lifts the uterus through the laparotomy wound, clamps the infundibulopelvic ligaments and divides them with a thermocautery. The uterus, thus mobilized, is raised high enough to suture the parietal peritoneum around the cervix. The abdomen is now completely closed in three layers including the skin, and the skin sutures covered with collodion. Only then the uterus is amputated with a cautery knife, the cautery being thoroughly applied also to the cervix surface.

Statistics prepared by Venus showed for the abdominal extirpation a mortality of 51.96 per cent, for vaginal hysterectomy 53.34 per cent i.e., practically no difference in the results obtained with either method. The mortality of 42.65 per cent for supravaginal amputation seemingly expresses the smaller risk inherent to this procedure.

The numerous antagonists of hysterectomy in the therapy of puerperal fever advance various reasons for their views. Branham, e.g., is certain that thorough emptying of the uterus with opening of posterior culdesac (Pryor's method) yields better results than radical interference. Carstens calculates that hysterectomy would be reasonable only for the advanced case, but if as a routine performed early, must occasionally cause the death of a patient who would have recovered if let alone. Kuestner asserts that he had never seen a patient on the postmortem table who in his belief could have been saved by him with a hysterectomy.

All the objections that have been raised against hyster-



ectomy can be easily summarized in but a few words: Difficulty of determining the indications for the operation; its dangers; the impossibility of deciding how far the process has progressed, and finally the natural aversion against a major operation to be performed on an extremely sick patient. To all this is added the utter impossibility of predicting whether or not this serious step really will improve the patient's chances of recovery.

Some writers base the prognosis on the blood picture. Recovery might be looked for if the increase of the polynuclear leucocytes is slight but that of the eosinophiles is marked. If the patient's resistance has become very low, the polynuclears are greatly increased in number (more than 95 per cent), while the eosinophiles are only slightly more numerous or indeed have disappeared (Deletrez, Cumpston). Lemoine concludes that the patient is unable to further defend herself against the infection when with a leucocyte count of 25,000 and above, the polynuclears continue to increase in number, and the eosinophiles continually become less while basophiles are absent. This, in his opinion, represents the time when the uterus should be removed. Also Guiccardi operates when the eosinophiles begin to decrease.

Our point of view in respect to the various aspects of this problem is the following: We heartily dislike extirpation of the uterus as part of the therapy of puerperal sepsis and consider the operation justified only in cases of necrosis of a myoma or of perforation of the uterine wall. It makes no difference in this respect whether this perforation was produced in managing an abortion or really is a uterine rupture occurring during or after labor. We proceed in this manner primarily because we desire to eliminate the danger of a severe hemorrhage or of a peritonitis. The opportunity of removing by means of the operation the source of infection is only of secondary importance for us

though it enters into consideration and to a certain extent influences the choice of the particular type of operation to be performed.

I might add in this connection a few words in regard to our principles of dealing with a uterine perforation. If there is no absolute certainty that the perforation has occurred under reliably aseptic conditions, we no longer rely upon mere suture of the wound, as we used to do, but we extirpate the uterus. We find that for this purpose supravaginal amputation usually is sufficient, of course, granted that the extent of the injury does not require the removal of the whole organ. Most of these cases reach the hospital within a very short time, while the infection still is limited to the area of perforation which will be the area of placental attachment. Since the placenta as a rule is located in the fundus, amputation of the corpus uteri will eliminate completely the infected area. If after amputation the posterior wall of the preserved cervix is split, drainage will be as effective as after a total hysterectomy.

The chief advantages of amputation over radical operation are the shortening of duration of operation and the avoidance of opening the innumerable veins and lymph channels in the parametrium.

We never had occasion to operate on a patient suffering from puerperal fever, on account of the retention of a placenta "which it was impossible to remove in any other manner." This indication for operation arises so early after labor that it really is part of the management of the still uninfected puerperal woman.

Abscesses in the uterine wall, which we have seen at autopsies, have never induced us to perform a hysterectomy for the very simple reason that we have never been able to ascertain their presence in a living patient. Some American writers claim that these abscesses can be diagnosed by palpation. We doubt that patients affected in

so serious a manner could ever survive so serious an operation.

Systemic infection in our opinion should be accepted as a strict contraindication against hysterectomy because the removal of the primary focus would not directly relieve the general infection, while the advantage of elimination of the possible source for further invasion of bacteria or toxins is likely to be more than balanced by the risks inherent to the operation. We know that some gynecologists maintain they have observed direct benefit from the removal of the primary focus of infections but for definite reasons we are not convinced of the justification of their claim.

We have no way of determining whether, and to what extent, the infection has spread over vessel or lymph paths, whether metastases already are established, of which each one anew represents a new focus of an importance equal to that of the primary focus. Dealing, e.g., with the bite of a serpent, we know that a definite amount of poison deposited in the wound gradually will enter the body. Prompt cauterization or extirpation removes the source of further intoxication and thus offers the body a much greater chance to battle with the poison already entered. In a case of puerperal infection, however, the primary focus sends into the body living germs, which produce more toxin as they multiply. Their deleterious activity will continue in spite of the elimination of the site of their origin.

How very quickly this process of propagation might occur in the case of a puerperal infection, every experienced obstetrician knows from instances in which a foudroyant sepsis rapidly developed which could not possibly have been prevented even by immediate hysterectomy. And in some of these cases, he saw the alarming clinical picture completely subside and the patient recover practically without any therapy, surely without surgical interference.

Practical experience continually proves that none of our present methods enable us to estimate the virulence of the offending germ, or its ability to multiply or to penetrate into deeper tissues. As long as our ignorance in this respect continues, we must be willing to accept a recovery after a hysterectomy as merely a fortunate coincident, leaving the question open whether in this instance it was inevitable to sacrifice the uterus. This situation is well illustrated in a recent report by Peri and Balard. In a case of puerperal sepsis hysterectomy was decided upon, but external conditions prevented its immediate performance. The next day the patient had improved to such a degree that it was decided not to do the operation. She recovered.

What I have said concerning hysterectomy for general sepsis applies as well to the proposition of removing the uterus for a bacterial endometritis.

How can we diagnose this condition? Negative blood culture and negative palpatory findings offer no clue. Negative palpatory findings, as already explained, do not exclude the possibility that some bacteria have already entered surrounding structures.

Outside of these evident obstacles to a precise diagnosis, we always felt unable to find the justification for hysterectomy for the better reason that a large percentage of these instances of endometritis certainly recover practically spontaneously. An operation might become responsible for the very scattering of germs one attempts to prevent. Again we except from this rule of noninterference the cases of necrotic fibroids and of uterine perforation. Prompt diagnosis and therewith prompt interference is imperative for these cases. Only then will the area of infection very likely be still circumscribed at the time of operation.

The foregoing arguments, I trust, explain satisfactorily our aversion against the removal of the puerperal uterus



and our acceptance only of a necrosis of a myoma or of a uterine perforation as justification for this operation. We feel certain that this attitude has brought no harm to any of our patients and we know of no instance when we felt ashamed at the postmortem table for not having removed the uterus. As a matter of fact, in 200 necropsies of patients dead from puerperal sepsis we have seen only four cases in which conditions might have been considered fairly favorable for a hysterectomy. This minimal percentage seems of no practical significance if we remember that the unfavorable conditions existing in all the many other cases could not have been clinically determined beforehand.

### Treatment of Peritonitis

**Operation.**—Decidedly more unanimity than in regard to hysterectomy can be noticed in the views of modern gynecologists concerning the treatment of puerperal peritonitis. With but few exceptions they are enthusiastic advocates of operation. Some difference of opinion, however, prevails as regards the following questions: When shall we operate? Which operation shall be performed? Shall the peritoneal cavity be flushed? How is best drainage obtained?

Gradually authorities concur in the view that the operation should be done just as soon as the diagnosis is made, but that interference is justified merely by a strong suspicion of peritonitis. "Early enough but not too late," says Leopold, and we agree with Latzko's advice to deal with a puerperal peritonitis exactly in accord with the now generally accepted rules for cases of ruptured extrauterine pregnancy.

The attitude of Sourdille seems to us unintelligible. He recommends a laparotomy for every serious case of puerperal sepsis, even in the absence of signs of peritonitis, be-



cause in this manner "the important and active area of absorption of toxins and bacteria is eliminated."

Discrepancy and actual contradiction prevail concerning certain points of technic. Nordmann, Koblanck, and Fromme insist on a long laparotomy incision, Bumm or Baisch prefer a short incision. Many surgeons follow the advice of Bumm and add flank incisions, others open the posterior fornix also, some combine them all (Masure, Koblanck, Leopold). Kownatzky prefers an incision in the inguinal region to the customary midline incision and often adds a counter incision in the flank or the posterior cul-de-sac.

Most gynecologists seem to follow Bumm's advice to reduce operative procedure to a minimum, resort to small abdominal incision and drainage, and avoid all heroic procedures (removal of uterus or other organs), to limit duration of operation as far as is feasible. Baisch repudiates the extirpation of any organs because thus many new entrance ports are opened for the infection. Only few writers regard the removal of the organ which is primarily responsible for the peritonitis, as indispensable (Hornstein, Fromme, Koblanck, and Jeannin). The latter recommends specifically the separation of all adhesions, to which Koblanck agrees, while the procedure is condemned by the majority of surgeons (Benthin).

**Flushing.**—In the question of flushing the opened abdominal cavity, both its defenders and opponents advance many weighty arguments. But each side concedes that under certain conditions the attitude held by the other is justifiable. Bauer, e.g., in early cases uses only gauze sponges, but the lavage in advanced cases; while Fromme prefers for a peritonitis of several days' duration the dry sponge and he never flushes.

Lavage, continued until the return fluid is clear, is recommended by Baisch, Hoch, Koblanck, Masure, Murat, Willis,

and many others. Kuhn employs a 4 per cent sugar solution because sugar furthers the formation of fibrinogen, inhibits secretion, proves nonirritating to endothelium and prevents the formation of alkaline toxins. After finishing with the thorough lavage, he pours into the abdomen before closing a small amount of a 10 to 20 per cent glucose solution. I think Burtenshaw goes too far in advising continuous lavage with a saline solution for one hour.

Like Bumm many refrain from all flushing (Kownatzky, Meyer, Boquell, Benthin, etc.). French authors have suggested injection of fluid in intervals of one to two hours through the drainage tubes, a procedure resembling continuous lavage. Saline solution, horse serum, also collargol have been employed in this manner.

While formerly it was the rule to flush with normal saline solution, more recently some authors feel that more than the mechanical effect of removal of secretions can be secured by making use of antiseptic solutions. A part of the fluid necessarily remains in the abdomen, thus exerting also a bactericidal effect. On this principle such preparations as yatren,<sup>1</sup> tryptaflavin,<sup>2</sup> vuzin,<sup>3</sup> or rivanol<sup>4</sup> now have been introduced also into the therapy of peritonitis. No definite information concerning results is as yet available. Schoenbauer reported very satisfactory results with an acetic acid-pepsin solution though only in cases of surgical peritonitis.

The pouring of ether into the opened abdomen, a method first employed by Broca and later highly recommended by Derganc, has found favor chiefly with surgeons. The

<sup>1</sup>See footnote<sup>3</sup> on page 58.

<sup>2</sup>3,6 diamino—and 100 methylacridiniumchloride. A yellow dye substance originally employed in trypanosoma infections, now extensively used also as local disinfectant.

<sup>3</sup>Isoktylhydrocuprein—The vuzinum hydrochloricum is soluble in warm water, formerly employed only as a surface disinfectant now also in form of deep injections, e.g., in mastitis. It is held to be a specific against gas bacillus. Usual concentration: 1 to 1000 and 2000. Causes at times local irritation, also headache, fever, exanthema.

<sup>4</sup>2 ethoxy—, and 6.9 diaminoacridinhydrochloride. A water-soluble yellow powder, in constitution, action and application similar to vuzin.

method gained a few enthusiastic advocates as well among gynecologists (Sigwart, Benthin, Koblanck) in the treatment of puerperal peritonitis, since they had become familiar with its efficacy in general surgical work which they were forced to do during the war. Ether (50 up to 250 c.c.) was at first used for its curative effect. Benthin asserts that by this method the mortality from peritonitis was reduced from an average of 70 to 80 per cent to 50.7 per cent (for cases of abortion to 36.8 per cent).

At present ether is recommended also as a prophylactic when during operation the peritoneum somehow has become contaminated with infectious material.

At first we held no definite opinion concerning the value of flushing. We used it in some instances and deliberately omitted it in others. Which are the possible dangers, which the advantages of flushing?

Undeniably it represents a simple and safe method of removing, without damage to the peritoneal endothelium, a large amount of pus, but not all of it. A considerable amount is unavoidably left behind, and therein lies the chief shortcoming of the procedure. The injected fluid never passes through all the folds, crevices and corners formed between the intestines and the other abdominal organs, and especially between spleen or liver and the diaphragm. These remaining pools of pus are not cut off from the rest of the peritoneal cavity and from them the infection invades the abdomen anew.

Saline solution left in the abdomen might be useful in raising a low blood pressure, but it does not, as has been suggested, stimulate peristalsis of the paralyzed intestines. For this purpose its concentration is too low, and its mechanical effect insufficient because it is simply permitted to flow in. Further experiments with hypertonic solutions would seem desirable in view of the investigations of Reschke which showed that solutions of higher concentra-

tion reduce for a short time resorption of bacteria and toxins, and thus possibly prevent the sudden inundation of the body with toxic material.

Flushing certainly might carry the infection into parts of the peritoneal cavity still intact. Dilution of the pus might actually favor resorption. Flushing continued until the return fluid is clear, or applied for one hour as advised by Burthenshaw, inevitably lengthens both operation and anesthesia. All these are disadvantages likely to void possible benefits.

For these reasons we discarded the flushing of the opened abdomen several years ago. We might introduce just a little saline solution if we find thick pus in a deep posterior culdesac, adhering too firmly to be wiped out with a gauze sponge. But then we do not fail to remove at once carefully the fluid, as we do thin pus, with a soft compress which will not injure the peritoneal surface. Most of the free pus will flow out when the wound edges are depressed and the pelvis is lowered.

Flushing persisted in until the fluid would return clear, we tried some time ago, but it was really never observed to happen. It might occasionally be possible, but even that would not prove that all pus had been evacuated. Autopsies offer ample opportunity for the evidence that often the stream of fluid has never reached considerable accumulations of pus in inaccessible nooks. For obvious reasons we cannot pass judgment on the special value of certain antiseptic solutions (of rivanol, vuzin, etc.) more recently recommended for peritoneal douching. We have administered such solutions in a few cases intravenously, but their failure even in this form of application, justifies no great hope that they could be very useful antiseptics when employed for the washing out of the infected abdomen. We have had no personal experience with the acetic acid-pepsin solution of Schoenbauer or with the Dakin solution.



Thoroughly dissatisfied with the results seen from the pouring of camphor oil into the opened abdomen, we discontinued this method of Glimm some time ago.

This might be the opportune place to mention experiments I made several years before the war. I decided to test, in cases of peritonitis, the effect of an animal coal emulsion poured into the peritoneal cavity. I thought the patient might be benefited in two ways: The coal might bind some of the toxic substances, and small particles might enter and thus block the peritoneal lymph pores, resorption in this manner being delayed or prevented. The patient then would be in a better position to win in her fight against the existing systemic infection. The trial was made in but a few cases, really not sufficient for a final judgment, but the results were far from encouraging. Some patients recovered; however, I do not ascribe this to the coal emulsion, as a matter of fact, the majority of them did not escape their fate.

Flushing through drainage tubes in the after-treatment also proved unsatisfactory in our hands. Adhesions form too readily, and soon the flushing amounts to not more than a cleaning of the tube and its immediate neighborhood.

More extensively we have tried ether. We failed to notice the marked reduction in the mortality rate that has been claimed especially by Benthin, but we admit that our own deductions are based on a material which cannot be compared with the imposing series studied by him. Like others we soon increased the 20 to 30 c.c., used at first, to 150 and 250 c.c. and pour the ether into the abdomen just before it is closed, or immediately afterwards through a funnel attached to the drainage tube. The immediate effect certainly is favorable. The pale and clammy skin of the patient becomes red and warm. The pulse becomes fuller and stronger, respiration slower and deeper. All this creates a picture quite different from that usually seen in



a woman who has just passed through an operation for septic peritonitis. This favorable general effect, however, unfortunately lasts but a short time and, in our own experience in contrast to that claimed by others, represents the sum total of the achievement. We have failed to observe that the peritoneal process took a markedly more favorable course, and if it occasionally did, we have no proof that this was owing to the introduction of ether.

What good effect could be reasonably expected from etherization? The ether could act as a bactericide, as it seemingly does in the experiments reported by Sigwart. Its area of efficacy might be extended by its ability of vaporization over the limits naturally inherent to any other liquid antiseptic. But it is improbable that even the ether vapor will penetrate into all the numerous crevices of the abdominal cavity and thus reach and destroy every trace of pus. Ether is devoid of any antitoxic power. Most patients suffering from a general peritonitis actually succumb to the intoxication, a blood stream infection can be ascertained only in a relatively small percentage of them. These toxins are either produced by the bacteria or the direct result of their disintegration. Such an inundation of the body with poisonous material, ether can prevent no more successfully than any other disinfectant. Even if the ether has destroyed microorganisms in large numbers, there will remain enough of them to continue toxin production. Theoretically, in peritonitis solely an agent which would exhibit an *enduring* antitoxic as well as antiseptic power, would prove of real value, but as much cannot be expected from ether because its effect is notoriously *fleeting*.

The reasonable argument might be raised, that this evanescence of ether could be overcome by repeated injections of the drug through the drainage tubes. This was suggested by Sigwart. Taking into account once more conditions to which I have repeatedly referred, ether reinjected

even only shortly afterwards will not reach the free peritoneal cavity any longer but solely a small pocket formed around the end of the drain. There is no chance that this ether at later injections would ever penetrate to more remote pus foci.

It has been asserted furthermore that ether vigorously stimulates peristalsis. Its intense cooling effect will cause the paralyzed gut to contract momentarily; this result will however, be of short duration and hardly be renewed by repeated injections for reasons just mentioned. Therefore, I consider of little practical importance the discussion whether ether hastens or prevents the formation of intestinal adhesions (Sigwart, Frankenstein). The short lasting peristaltic contraction can hardly prevent adhesions. Whether ether favors the development of adhesions is a problem of no significance for cases of peritonitis in which pus and exudate by themselves inevitably lead to their rapid and extensive formation.

Evident and important, however, is the good effect of ether on circulation which I emphasized in the beginning of this discussion. The chilling causes a contraction of the blood vessels in the intestines and mesentery, and temporarily reduces the existing abdominal plethora. More blood being thrown into circulation the heart action becomes more effective, which necessarily was impaired by the narcosis and the operative shock. The resulting improvement is objectively noticeable.

My personal experience is decidedly limited in respect to certain shortcomings of ether in cases of peritonitis, but ether applied in this manner has been held responsible for such complications as tachycardia, (Frankenstein), pulmonary complications and shock.

We never observed a case of real shock but always an increased deepening of the anesthesia. This, however, is probably not important because we always try to maintain

the anesthesia during an operation for peritonitis rather superficial and "intermittent," making it deeper only while the peritoneum is opened and later again when it is closed. Since we are acquainted with this peculiar effect of the ether treatment, we are doubly careful to apply the ether most sparingly on the mask so that the subsequent deepening of the narcosis can do no harm.

We would hesitate to blame definitely the ether poured into the abdomen for a fast pulse, a bronchitis or any other pulmonary complication because these certainly represent not very uncommon sequelae of a peritonitis.

In summarizing our own experience with etherization of general peritonitis I can record solely an immediate and brief effect on the circulation and general condition of the patient but no definite, favorable influence on the course of the disease. It is possible that these conclusions might be influenced by the fact that we have not employed the method in a very large number of instances since even now we resort to it only in special cases.

**Drainage.**—Justly the necessity of effective drainage is emphasized by all writers. Unfortunately all efforts in this respect so far have failed to solve the problem. Complete removal of all secretions is technically impossible.

Most gynecologists drain, as is taught by Bumm, through the incisions in midline, in flank and in posterior culdesac. Some insist that it is risky to keep the communication between peritoneum and vagina open with either gauze strips or a tube (Franz, Hirst).

There are those who prefer the drainage tube, sometimes with special curves and bends, and others who consistently employ the gauze strip. Still others make use of both means, either introducing them side by side, or winding the gauze around the tube.

These differences are of no particular consequence. They all express the desire to drain thoroughly and indicate the

endeavor to achieve this end more successfully by still another modification.

The advice, coming in the main from surgeons, to close the abdomen completely without any drainage, so that normal intraabdominal pressure will be restored, has met with but little approval among gynecologists.

Drainage solely through the vagina in cases of diffuse puerperal peritonitis, though practiced in America and also in France, has been approved in Germany by few outside of Doederlein. Cardot thinks highly of vaginal incision for diffuse peritonitis because it is a simple operation, easily done, which affords excellent drainage. This idea originated with Pryor who expected that the prompt removal of the peritoneal fluids would protect the general system against intoxication. He gave the following rules: In lighter cases, when streptococci, staphylococci or *Bacterium coli* is found in the uterine secretions, the uterus is thoroughly washed out and then packed with 10 to 20 per cent iodoform gauze. If this procedure is not followed by prompt improvement, Pryor assumes that germs already have passed beyond the uterus. This opinion is based on the observation that under these conditions fluid obtained through a promptly made fornix incision always contains bacteria. He brings iodoform gauze into the uterus for the specific purpose of causing an absorption of iodine into the system. To prevent a marked general iodism, copious enemas or subcutaneous infusions with saline solution must be made. The urine should be examined every three hours for its iodine content to control the efficacy of the procedure and also the elimination of the absorbed iodine. Usually the procedure leads to a chill followed by a fall of temperature which from then on remains low. The uterine packing is removed after three days, Douglas drainage after eight days. Pryor's method is considered by Brinkley as the best now available.



In all drainage methods great stress is placed on the after-treatment. I have mentioned the repeated injections of fluid through the tubes. They are intended not only to keep the tubes open but also to introduce substances with curative properties into the drained cavity. These injections probably serve the former purpose well but are not likely to prove very effective for the latter. We had occasion in foregoing pages to consider the doubtful therapeutic value of antiseptics, serum, collargol, etc., in the treatment of puerperal infections. If injected through a drainage tube these substances will most likely reach only a rather circumscribed part of the affected area on account of the adhesions which promptly form around a drainage tube. This walled-off cavity around the drain end furthermore is covered with fibrin deposits which necessarily interfere with any direct action or resorption of the injected fluid. Saline solution however valuable when given subcutaneously, intravenously or rectally, therefore will fail to exhibit any beneficial effect when introduced through a drainage tube.

The view of Gilliani concerning the *modus operandi* of a rectal administration of physiologic salt solution seemingly has not appealed to other clinicians. He believes that saline, given in form of the rectal drop, fills the lymph spaces so that neither bacteria nor toxins can pass through them. In his opinion the rectal drop actually protects the body against intoxication. Gilliani also stresses the necessity of elevating the head end of the bed, which causes the exudate to gravitate into the lower pelvis whose peritoneum has less absorptive power than the upper peritoneum near the diaphragm. This position, actually introduced by Fowler and Murphy, probably does not act in the sense suggested by Gilliani, but nevertheless has its definite advantages. It certainly favors the escape of pus through an opening in the posterior culdesac and might lessen resorp-



tion because pus within the small pelvis is more likely to become walled off by adhesions. There is no evidence available for the assumption that the pelvic peritoneum possesses less absorptive ability than that of the upper abdomen.

The addition of adrenalin to the saline solution is particularly advantageous when the blood pressure has suddenly dropped, a phenomenon which has been explained on the basis of the degenerative changes in the adrenals very frequently observed in cases of peritonitis. This effect, however, is not specific. Pituitary preparations will yield the same good results.

It is obvious that in every case of peritonitis heart action and peristalsis should be stimulated by suitable medication, and that the patient be properly nourished.

Our own routine in dealing with puerperal peritonitis is the following: The definite diagnosis of peritonitis represents the strict indication for operative interference. Excluding those patients who apparently offer not the slightest hope for recovery, we perform a laparotomy in every case in which we observe the development and further progress of a peritonitis under our eyes in the clinic. If a patient is admitted with the symptoms of a beginning peritonitis, which seemingly has not spread into the upper abdomen, we are willing to wait, because experience has taught us that in such cases, sometimes the process remains limited. A circumscribed abscess might form, and then it is easily opened through the vagina. Immediate laparotomy in such a case would not only preclude the formation of a localized abscess in the pelvis but indeed is apt to carry the infection into the still intact upper abdomen.

Certain clinical observations guide us in deciding whether or not the process is likely to terminate in encapsulation.

We have found that circumscribed localization of the

process can be looked for if a shallow groove across the abdomen, usually at the level of the navel, separates the affected lower from the still intact upper abdomen. While the lower part is distended, tense and tender, the upper remains soft and flat. If this groove or depression is well marked, a favorable prognosis can be made. These are the cases which later might be quickly benefited by a vaginal incision, and many of them recover without any operation. To these cases Murphy's terse advice most aptly applies: Get in quickly.

Rather generally the opinion prevails that a streptococcus peritonitis shows no tendency to localize. This is not borne out by our numerous observations of pelvic abscess formation under these conditions, especially after abortions, and we feel that in a definite percentage of cases one can count on such a happy development.

If the peritonitis is diffuse we exclude, as already mentioned, only moribund patients from a routine laparotomy. If performed promptly this operation can do no harm but at times results in considerable benefit. We fully realize that this strict demand of performing the laparotomy promptly in practice cannot always be carried out. Puerperal peritonitis, "of our own making" in clinical patients, fortunately has become a rarity. Patients admitted to the hospital from the outside, however, hardly ever reach us before the third or fourth day. We might operate upon them immediately after admission, but we cannot term this "early operation."

The main symptoms on which we base our diagnosis and thus the indications for interference are: small and fast pulse, tenderness of entire abdomen, often dull percussion sound in flanks, distention of abdomen, and general rigidity of the abdominal muscles, a symptom always present with the exception of the patients *in extremis*.

After various modifications we have at present adopted

the following technic: Median incision from symphysis to almost the navel. Usually this permits a larger or smaller quantity of pus to escape. Without lengthening the operation unduly, all adhesions between intestinal loops and genitalia as far as possible are separated. In contradistinction to the views of some operators, we lay great stress upon this point, because at postmortem we have often observed that, with the rest of the peritoneum well cleared, such walled-off pockets would still contain a considerable amount of pus. While they presumably do not act in turn as primary foci for further spread of the infection, they undeniably impair the general condition of the patient as sources for continued resorption of toxins. We do not insist on a careful examination of uterus and adnexa except when we have to search for a suspected uterine perforation, simply because, as amply explained in foregoing paragraphs, we object on principle to any extensive operation, exempting from this rule alone the perforated uterus. In view of the meteorism, always present in these cases, exact exploration of the internal genitalia furthermore would require a very deep anesthesia, which would unavoidably increase the risks of the interference.

Counterincisions we make often but not, by any means, always. For this purpose we take our choice between the inguinal region and the lowest point in the flank at the level of the iliac crest, but occasionally place them high up close to the costal arch. A counterincision is usually omitted if we find but little fluid exudate as in the very unfavorable type of dry peritonitis, when the serosa is hyperemic and covered either with a fibrinous exudate or sometimes with flat blood clots from petechial hemorrhages. We hold a similar attitude in regard to the opening of the posterior culdesac, which in our opinion can be of advantage only if a considerable amount of pus has accumulated behind the uterus.

Major operations for the removal of the original starting point of the peritonitis, for total or partial extirpation of the genitalia, we have not performed for the past several years. We used to be more radical, but experience with a large number of cases has taught us that conservatism in this respect is the safer plan, although we have seen some of these patients recover "in spite of the operation." We never could convince ourselves that the operation saved the patient's life, that she would not have recovered without it. The general rule must be, not to overtax such a patient with a serious operation when her resistance is so markedly lowered.

Baisch's reason for objecting to operation—increased danger of resorption from the pedicle stumps—does not appeal to us since the lymph channels of the immediate neighborhood as a rule will already be infected, and the slight plus of increased chance of further resorption could be neglected in the face of the definite minus of resorption effected by the free drainage.

A most difficult and most baffling problem in the treatment of peritonitis is that of effective drainage. In regard to the choice between the tube, the gauze strip, or a combination of both, experience at the postmortem table has revealed to us various shortcomings of each method but has not offered us any definite clue as how to eliminate them.

At first we adopted the rule to run drains from the wound towards liver, posterior culdesac and into the flanks, distributing furthermore gauze strips through the abdomen in various directions. The effect was uniformly unsatisfactory, the drainage always insufficient. If such patients came to necropsy within a few days, the findings were such as one should naturally expect. Underneath the drainage tube a groove had formed, in and over which adjoining tissues were fastened together by adhesions, resulting in the



formation of a sort of channel. The openings at the end of the tube and likewise those cut into its side wall were clogged with masses of fibrin protruding into the lumen of the drain. This, of course, precluded any possibility of their functioning in the expected sense and indeed very often a veritable pool of pus was surrounding the end of the drain. When the drain is covered with gauze this clogging is prevented or at least delayed. This addition of gauze, however, does not procure drainage of a wider area because the gauze as well leads to the formation of adhesions and thus to a sort of encapsulation of the strip.

Gauze strips by themselves at least are an ideal means of drying up a definite region. The beds in which they are lying are found free of fluid contents or pus. But gauze stimulates the development of adhesions and therefore their inherent ability to drain from a wider area ends as soon as a well-defined pocket is formed or when they have become soaked and thus lost their absorptive faculty. For this reason they prove of great value only in the treatment of localized foci, e.g., in an appendiceal abscess. In the therapy of a general peritonitis their usefulness is limited.

The Mikulicz drain, a bag of gauze stuffed with strips of gauze, offers no advantage over the individual strips because its gauze cover entails all the drawbacks inherent to this material.

Cigarette drains, made by wrapping a smooth material such as oil silk or thin rubber around gauze strips, are less prone to cause adhesions but in the end will produce them, and then again they will drain but a well circumscribed pocket. Their most evident advantage consists in the possibility of removing them with comparatively little discomfort to the patient.

It seems irrelevant whether the drainage material is led out through the abdominal wound or through a vaginal incision. But if there is a good deal of liquid exudate and



the patient can be kept in the Fowler position, the culdesac represents as the lowest portion of the peritoneal cavity a point of vantage for successful drainage.

Clinical observations and pathologic-anatomic studies have prompted us to use most extensively the gauze drain. We never employ the tube alone, and if at all, only either wrapped in gauze or paralleled with gauze strips. We run gauze strips from the wound into all accessible portions of the abdominal cavity, pushing them with long forceps high up towards stomach and liver and over to the spleen. The results of this technic are not entirely satisfactory, obviously since the effect of each strip is strictly local. Those areas that are not directly reached by them remain uninfluenced and a laparotomy incision, even if carried up to the navel, does not afford access to every part of the abdomen. To achieve really perfect drainage complete even-tration would be inevitable. Two definite reasons exclude any such attempt. The shock incident to it would prove too great for most of the patients. Reposition of the intestines would require a very deep anesthesia which is strictly contraindicated for these patients. It might be possible in some instances to close the wound in the lower abdomen and then to make a further incision from navel up to the ensiform process. In this manner the organs in the upper abdomen could be reached and the pus removed, but this still would preclude any possibility of draining all the innumerable spaces between the individual loops of intestines. Theoretically at least it must be admitted that this added drainage of all pockets between stomach, liver and diaphragm might better the patient's fighting chances but the presence of so very many gauze strips, on the other hand, undoubtedly would later necessitate a general anesthesia for the removal of some of them. Trials with such an extensive procedure might be justified and might eventually determine its value. This one thing seems evident:

The problem of a perfect drainage in general peritonitis is far from its final solution for which much painstaking work and thought will still be required.

So far we have not had the courage to desist from all drainage, as recently has been suggested by some surgeons. Drainage, though not ideal or lasting in its effect, at least removes a considerable amount of pus. It leads to adhesions and thus to a localization of the infection; as a foreign body in the abdomen, a drain, or gauze strip might stimulate circulation and peristalsis. If we close the abdomen completely without drainage, we know that the patient now has to battle not only with the pus left within the abdomen, but also with that which will form afresh.

In dealing with general peritonitis in a puerperal woman, we are not sharing the usual advantage of the surgeon who is able to remove the primarily diseased organ and thus shut off any further ingress of toxic material. The gynecologist has learned by sad experience that for his work the smallest operation, laparotomy and drainage, is the best. There might be a definite advantage in quickly restoring the normal intraabdominal pressure by closing the wound completely, but its reduction will be only slight if, as is the custom with the gynecologist, the abdomen is closed with the exception of the relatively small opening required for drainage. It is not quite clear why one should place more faith in the "physiologic autoprotective ability of the peritoneum" which in a case of diffuse peritonitis certainly must be greatly impaired, than in the natural resistance of e.g. a phlegmonous extremity. In the latter case it would seem quite improbable that a surgeon would attempt to close hermetically at once the incision he has made.

In regard to vaginal celiotomy for a diffuse general puerperal peritonitis we have no personal experience. But we readily make use of this operation when we find an abscess localized in the pelvis. A T drainage tube left in the inci-

sion has proved very effective in many cases of this sort. It seems possible that through it pus might escape, in so far as it has not become walled off by adhesions, but this really means that on the whole its effect on the exudate lying higher up in the abdomen is negligible.

For reasons which seemed valid to us, we have never tried Pryor's procedure. First, the mere finding of certain bacteria in the uterus by itself does not call for therapeutic interference because we could ascertain this condition as well in innumerable cases of afebrile puerperium. Furthermore, we object on principle to all intrauterine manipulation in a case of puerperal fever because we believe it is too apt to do actual harm. On the other hand, we regard the necessity of opening and draining the culdesac in the presence of a pelvic abscess as self-evident. The iodization of the patient seems an unnecessary adjunct of the procedure in case of a localized process, and certainly is valueless if the entire peritoneum is involved. The small amount of iodine resorbed from the gauze strips can be of no importance as a curative remedy for the blood infection, since even larger doses of iodine, administered subcutaneously or intravenously, have been found void of value.

A few more words must be said concerning the anesthesia. We open the abdomen under a superficial general narcosis, occasionally under local infiltration, and have occasionally also employed spinal anesthesia. As most favorable we consider a general anesthesia with ether. Infiltration of the abdominal wall, most desirable in view of the common cardiac impairment, offers so little pain relief as soon as the peritoneum is opened, that as a rule a general anesthetic must be administered to stop the patient from straining and to enable one to explore the abdomen. Medullary narcosis insures complete absence of all pain and as perfect a relaxation of the abdominal wall as can be obtained only by means of deep chloroform anesthesia. Thus it offers

ideal conditions for thorough examination of the entire abdomen and proper placing of all drainage strips. Willingly and often we make use of this method in our general surgical work but try to avoid it in operations for a diffuse peritonitis because we have gained the precise impression that just these patients after operation seem generally in a far better condition after ether than after medullary anesthesia. The beneficial effect of the ether on circulation and respiration to us seems beyond any doubt though admittedly this benefit is but of short duration. Possible damage to the lungs from the ether is too rare to influence our conviction that for this operation ether represents the best anesthetic. Stimulation of peristalsis by lumbar anesthesia, as claimed by Wagner, we failed to observe.

We have never tried sacral anesthesia for these operations. Manipulations required for its administration, in our opinion, might seriously affect the very sick patient, and it also seems doubtful that its anesthetizing effect would extend high enough to permit handling of the organs in the upper abdomen.

**After-treatment (Saline Solution, etc.).**—The final outcome of the operation depends not more on its performance at the proper moment than on the care bestowed in the after-treatment. First consideration must be given to the patient's resisting power. Appropriate medication in this respect will greatly enhance the chances of recovery. The most important tasks are stimulation of heart action, restoration of peristalsis, and improvement of general condition.

Saline solution is the sovereign remedy to support the heart. We make extensive use of it, administering it usually in small quantities either subcutaneously or intravenously, more or less as a vehicle for other excitants, chiefly adrenalin or pituitrin, but are afraid that large quantities of the solution might overburden the heart. It is for this



reason that we prefer on principle the rectal drop, about 1000 c.c. within one or one and a half hours. The fluid is resorbed slowly without any possible strain on the heart. From 3000 to 4000 c.c. can be given in this manner, sufficient to keep the blood pressure at a higher level and to alleviate thirst. We do not expect the saline to block the lymph channels against bacterial invasion, as has been suggested by Gilliani. Cesol (Merck)<sup>5</sup> we have not found of particular value in relieving thirst.

Schoenbauer recently has reported that in experiments he has observed intravenous saline infusion to retard resorption. We have had no personal experience in regard to this observation, but if it should be correct it would represent rather an advantage than a disadvantage, and might offer still one more explanation why saline proves so useful in these cases. As already emphasized, it is exactly the foudroyant toxin resorption which represents the most deleterious element in peritonitis by rapidly impairing the heart and general circulation.

To raise the low blood pressure we add adrenalin to the infusion fluid (1:1000 solution) and more often hypophyseal extract, or give either one of the organ extracts without saline intravenously. The immediate effect can readily be noticed by the strengthening of the pulse. Unfortunately this beneficial result is of limited duration but hypophyseal extracts in particular can be injected repeatedly, several times a day, without any possible harm and thus a more lasting effect will be obtained.

It requires no further emphasis that the action of the cardiants must be supported by digitalis preparations, by camphor or caffein, liberally employed. In certain cases strychnine is specially indicated, either alone or in combi-

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<sup>5</sup>It is the brom-ethylate of methylhexahydropyridincarbonic acid methyl ester in form of hygroscopic crystals. It stimulates salivation and in this manner is supposed to relieve thirst. It is claimed that the effect is evident a few minutes after its hypodermic injection and will last for four to six hours. Occasionally it also causes profuse perspiration and nausea.



nation with strophanthin or a similar drug, and I may add, in our experience it is not necessary to administer these substances intravenously. One or repeated doses as a rule bring about well marked improvement of heart action. We assign an important place in the after-treatment of peritonitis to morphine which acts not only as an analgesic but also as an efficient cardiac stimulant. At first sight this might seem paradoxical, but in very many instances we could see how with ceasing restlessness of the patient and improvement of the discomfort from dyspnea, the heart function improved. The morphine had eliminated factors which were seriously impairing its action.

There are several possibilities of combating the ominous paralysis of the bowels. Unfortunately, efforts in this direction usually yield only limited results. First, as a rule, we try the electric light arc for a short time. Next we give high enemas with a soap sud solution, to which we add salt and glycerin, also with decoctions of senna leaves. If they prove ineffective, as too often is the case, we give hypodermic injections of physostigminum salic. (1.5 mg.) and pilocarpine (5 mg.). At times this causes gas and stool to be passed, often 30 to 45 minutes later a high enema is required to obtain a satisfactory bowel movement. All this can be repeated as required. We have never found hormonal<sup>6</sup> or neohormonal useful in our hands, and having observed occasional unfavorable sequelae we have completely discarded these remedies. Pituitrin in this respect is also very reliable.

Peristaltin<sup>7</sup> and other similar cathartics on the market

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<sup>6</sup>Hormonal is a spleen extract which according to Zuelzer, when introduced into the blood stream, causes strong intestinal peristalsis. This result is obtained between fifteen and thirty minutes with intravenous, between two and three hours with subcutaneous administration. It is advisable to give at the same time a cathartic. Very often the remedy is accompanied by undesirable by-effects, such as pain, fever, alarming rise of blood pressure and it is claimed that in some instances it was responsible for the death of the patient. Neohormonal is supposed to be free of the substances responsible for these objectionable consequences.

<sup>7</sup>A glucosoid prepared from the bark of *sagrada* (*rhamnus purshiana*). A yellowish-brown powder, soluble in water.

for hypodermic use have too mild an effect, though nausea and vomiting as a rule preclude the oral administration of other cathartics.

If all these efforts fail, we delay no longer to make an opening in one or even several loops of intestines. If a distended loop can be recognized in the upper abdomen we place the incision at the level of the navel or a little lower, otherwise the region of the cecum is the site of predilection. After thorough local infiltration an incision is made through the entire thickness of the abdominal wall. The first distended loop seen is lifted out and a circular portion of its wall, about one and a half cm. in diameter, sutured all around to the wound. A small slit is immediately made through the intestinal wall and a drainage tube slipped into its lumen. There is great advantage in avoiding the upper portion of the small intestine since otherwise later on the signs of inanition are prone to manifest themselves. Most favorable is an artificial fistula of the ileum.

The immediate effect of the fistula often is amazing. Stool and gas fairly gush out and the gut collapses. If the artificial anus actually functionates satisfactorily one is almost justified to prophesy that the patient will recover. Normal bowel function then usually is restored in a few hours or days, stool begins to be evacuated in good amounts *per vias naturales*. The drain can be extracted and the opening will close spontaneously.

Quite different is the clinical picture in the cases in which the prognosis is less favorable. Only a little stool and a few gas bubbles escape, the meteorism persists. At times conditions become a little more satisfactory when fluid is flushed into the bowel through the drain, or the latter is pushed deeper into the opened loop. But when even this does not help, then the patient might be regarded as lost.

Occasionally we can almost anticipate whether or not

the artificial fistula will prove helpful. It is very likely to be most effective if one can hear the gas escape through the tiny needle holes before the intestinal incision is made. The phenomenon proves that the tapped loop is not completely paralyzed and that there is a chance for it to resume normal peristaltic contractions.

In contradistinction to Novak and others, we do not believe in the advantage of opening the bowel at once. We have followed this plan only in a very few cases of excessive meteorism seen during the past years. We greatly prefer to wait with this operation because in quite a number of cases, surgical interference is rendered superfluous by medical therapy and because enterostomy is an operation of sufficient dignity not to be performed without serious consideration, although the artificial anus can be closed easily under local anesthesia.

Capillary puncture of the intestines we have done occasionally when resorption seemed very slow, but it does not relieve meteorism and in our opinion can be disregarded as an effective method of treatment.

The general condition of the patient we endeavor to improve by means of concentrated, nourishing food, also some alcohol. All the symptoms of peritonitis stand in so close a relation to each other that the relief of one usually also implies the alleviation of another. For instance, if we can improve the heart action to such a degree that the hyperemia in the splanchnic area is controlled, automatically also the intestinal paresis will be lessened. Restored peristalsis will promptly be followed by marked general improvement.

**Results.**—Very little can be said concerning the prognosis. The main deciding factor is whether there is solely a peritonitis or, coincidentally, also a complication with a general sepsis. In the latter case, in our experience, the outlook is extremely serious. In a case of peritonitis with-

out sepsis the outcome depends upon the ability of the heart to withstand the added strain, and our competency to restore bowel function. If we succeed along both lines the patient can be considered saved; if we fail, she will succumb.

The percentage of cures in our own material is disappointingly small. We are unable to boast with such results as are claimed by Latzko, Benthin and others. Of 142 patients on whom we operated we lost 83.81 per cent, and saw recover, only 23, i. e., 16.19 per cent. In cases of peritonitis with sepsis our mortality was 100 per cent. Of considerable importance for the prognosis is the time of operation. When we had been able to operate within twelve hours after the onset of the peritonitis recoveries amounted to 32.14 per cent, operations performed within twenty-four yielded only 25.45 per cent of cures, between twenty-four and forty-eight hours 17.78 per cent, between forty-eight and seventy-two hours only 7.69 per cent. Not one patient operated later than seventy-two hours recovered. These figures clearly establish the advantage of early operation.

These thoroughly disappointing results of the therapy of peritonitis become comprehensible if one recalls the enormous area of peritoneal surface involved by the infection as revealed at autopsy. Imposing quantities of pus usually are found between diaphragm and liver or spleen and large walled-off pockets of pus are discovered between the loops of the intestines and in the posterior culdesac. The extent and wide distribution of these foci can leave no doubt why the operative therapy must necessarily prove insufficient.

More promising and usually very satisfactory proves the small and relatively harmless incision made in the posterior fornix which opens a localized pelvic abscess and affords a free outlet for the pus accumulated there. It is of great importance, however, that through this incision



during operation all the various pus cavities are opened. It is entirely insufficient to drain solely the one pus sac lying in the space of Douglas. As a rule the pelvic pathology comprises more than this one pus sac. A pelvic abscess might be divided into several chambers by septa and there might also be present a pyosalpinx in one or both tubes. But rarely is it possible to ascertain these details by examinations made before operation.

With finger introduced through the vaginal wound one will feel the rigid wall of a pyosalpinx which, under guidance of this finger, can be perforated with a sharp-pointed instrument, such as a forceps. On withdrawal it is spread wide open to enlarge the incision. It is advisable at the moment of the perforation to push the mass from above against the instrument, by pressure through the abdominal walls. All septa must be carefully destroyed. One or two drains, adjusted with T or club-shaped ends, are introduced deep into the cavity. Their further fixation with gauze strips is usually superfluous.

Experience has taught us however that in rare instances it is preferable to refrain from any attempt to break up all the septa and to be satisfied merely with the incision. This is especially true for septic abortions when the exudate begins to accumulate soon after emptying the uterus. Too radical a procedure in these cases seems to favor the spread of the infection to the rest of the peritoneum. The adhesions upward probably are not yet dense enough to withstand the trauma of brusque manipulations incident to thorough exploration, and disregard of this precaution may have deprived many a patient of her chance of recovery. The localized peritonitis had been changed into one of the dangerous diffuse type.

As already stated, for the patient with a circumscribed pelvic peritonitis, vaginal incision usually proves sufficient and but rarely additional laparotomy is required. In the



few instances where this combination cannot be avoided we attempt to establish, by means of a long vaginal forceps, a communication between vaginal and abdominal incision, and on withdrawing the forceps pull a long drainage tube from the abdomen into the vagina.

The time when a vaginal drainage tube can be removed varies and is determined by the course the disease is taking. In some cases 14 days and less is sufficient, in others it must remain for several weeks, at least as long as the free discharge of pus continues. These drains annoy the patient but little, if at all. Under favorable conditions such patients might be discharged from the hospital with the drain still in place. When all secretion stops the tube is removed.

Various details of our technic and results are well illustrated in the few case histories which I shall quote briefly.

W. H., twenty-five years old. Admitted April 26, 1918, died April 28, 1918.

*History.*—Last menstruation early in February. Three days ago aborted. Digital evacuation of uterus. Since then has abdominal pain and constipation.

*Status pres.*—Temp. 37.8° C., pulse 144. Tongue coated, dry. Respiration fast, superficial. Abdomen greatly distended, uniformly tender. Vaginal hemorrhage. Uterus somewhat enlarged, soft.

Patient is given physostigm. salic. 0.0015 gm. and philocarp. mur. 0.005 gm. Some stool and flatus passed but distention and pain remain unchanged. Therefore soon afterwards laparotomy performed. Large amount of pus removed with saline flushing (several liters of solution). Loop of small gut is fastened to edge of laparotomy incision and, after closure of wound, is immediately opened. Fistula does not functionate well. Three gauze strips had been placed in abdomen. Next day abdomen soft and not tender. Subjectively, patient better but heart action remained poor in spite of stimulants. Exitus on April 28, 1918.

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T. M., forty-three years old. Admitted March 7, 1918, died March 8, 1918.

*History.*—Three days ago spontaneous delivery. One day post-partum, fever and chill. Severe pain in abdomen.

*Stat. pres.*—Temp. 38.5° C., pulse 132 medium full. Tongue dry, coated. Abdomen diffusely tender, walls tense. Uterine fundus midway between symphysis and navel, not distinctly palpable. Cervix open for finger.

Physostigmin and phloecarpine injection followed by passage of a little stool and some gas. Vomiting continues, therefore immediate laparotomy. Pus sponged out, no flushing. Primary fistula placed into lowest portion of ileum. Not functioning well. Abdomen closed.

No improvement. Patient died next day.

Better results are obtained if the fistula is made only a few days after the laparotomy when persistence or recurrence of meteorism necessitate this operation. It occasionally seems to save a patient. I shall refrain here from quoting such histories.

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M. R., twenty-six years old. Admitted March 18, 1915, died March 19, 1915.

*History.*—On March 12 spontaneous partus. Since March 14 pain in abdomen, fever and chills.

*Stat. pres.*—Temp. 37.7° C., pulse 120, frequent respiration. Lower abdomen greatly distended and tender, both symptoms less marked in upper abdomen, but no furrow recognizable between the two portions. Purulent discharge from vagina. Uterus poorly involuted. Enema not followed by either stool or gas.

Laparotomy. Intestines greatly injected, good deal of greenish, fetid pus in abdomen. Both tubes thickened, containing pus. Uterus large and soft.

Supravaginal amputation of uterus with bilateral salpingo-oophorectomy. Posterior wall of preserved cervix is split. Drainage both through vagina and abdominal wound.

Patient survived operation half a day.

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A. S., nineteen years old. Admitted July 27, 1914, died July 31, 1914.

*History.*—Last menses end of April. Bleeding for two days, passing shreds of tissue. Curettage.

*Stat. pres.*—Postabortal state. Slight hemorrhage. Ergot.

July 28. Abdominal pain, diarrhea, slight meteorism. Some tenderness to pressure over abdomen.

July 29. Subjective discomfort more pronounced. Meteorism and abdominal rigidity increased. Frequent vomiting. In view of the diagnosis of peritonitis, immediate laparotomy was done.

Great quantities of pus all over abdominal cavity. Bilateral purulent salpingitis. Uterus enlarged, soft, has a yellow tinge as if permeated by pus.

These findings, in spite of youth of patient, seemed clearly to justify a total hysterectomy, which was performed.

No improvement, patient died on July 31, 1914.

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U. E., twenty-four years old. Admitted May 7, 1913, discharged, cured, July 17, 1913.

*History.*—On May 2, apparently spontaneous abortion. Since admission to hospital pain in abdomen. Vomiting. No stool or flatus passing.

*Stat. pres.*—Temp. 39.2° C., pulse 122. Abdomen slightly distended. Lower abdomen markedly, but upper abdomen only slightly tender to pressure. Ill-smelling discharge. Uterus enlarged. Adnexa free.

Same afternoon condition unchanged.

During night excessive distention of abdomen, vomiting, intense pain. Therefore laparotomy.

Only in pelvis a little pus found. Both tubes of a dusky red color. From the right tube trace of pus can be expressed. Uterus enlarged, soft, probably still contains remains of the ovum. For this reason total hysterectomy including both tubes and ovaries was done. Drain into vagina. All stumps covered with peritoneum and abdomen closed.

Convalescence satisfactory. Patient discharged well on July 17.

It seems that in this case, in spite of the alarming symptoms of a diffuse peritonitis at the beginning, the operative findings strongly suggest the possibility that the process would have become localized. It would have been better in this instance to have refrained from an operation. Most likely the patient would have recovered as well and presumably in a much shorter time. This patient, we assume, recovered in spite of the operation as the result of her good general condition.

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K.R., twenty-nine years old. Admitted Nov. 2, 1913, discharged cured, Dec. 29, 1913.

*History.*—Aborted on Oct. 22. Curettage. Ever since has had chills, continuous fever and abdominal pain.

*Stat. pres.*—Temp. 37.2° C., pulse 84. Tongue dry, slightly coated.

Abdomen distended, somewhat tender. Mucopurulent discharge. Uterus retroposed, elongated, firm, not clearly distinguishable from a large mass of exudate reaching up to navel.

In view of fairly satisfactory condition, operation was not considered advisable.

Next day, suddenly very intense abdominal pain and frequent vomiting. Entire abdomen exquisitely tender. Pulse 140, thready.

Diagnosis of diffuse peritonitis made and laparotomy performed. Abdominal wall and preperitoneal fat are edematous. Through opening in peritoneum a great deal of pus fairly gushes out. Everywhere in abdomen, under liver and spleen, greenish, fetid pus. Intestines deeply infected and covered with fibrin. Great deal of pus in pelvis. Poor condition of patient precludes any major operation. Pus carefully wiped out with sponges. Drainage strips introduced into all directions and before closing, about 1000 c.c. of an animal coal emulsion (Merck) poured into abdomen.

After operation much stimulation required especially on account of deficient heart action. For several days digalen and other cardiacs administered, also physostigmin and pilocarpine for meteorism.

On eighth day sutures removed and some of the drainage strips extracted. Free drainage continued for several weeks, subsiding very gradually.

Patient discharged well on Dec. 29, 1913.

This case at first showed the signs of possible localization. No furrow, however, could be observed at any time which in other cases had clearly indicated to us a beginning localization of the process within the pelvis. Actually a diffuse peritonitis finally developed, not through rupture of a pus tube but as result of direct propagation of the infection. Following our rule the least serious operation was done. How much the coal emulsion added in the recovery remains an open question. It might have helped resorption.

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T. G., twenty-seven years old. Admitted Feb. 16, 1914, discharged cured March 28, 1914.

*History.*—On Feb. 1, spontaneous delivery. Since then profuse, ill-smelling vaginal discharge. On the day of admission began to complain of abdominal pain.



*Stat. pres.*—Temp. 37.3° C., pulse 108.

Abdomen somewhat distended, slightly tender. Mucosanguineous discharge. External os closed. Uterine fundus three fingers above symphysis.

Feb. 18. In afternoon suddenly intense abdominal tenderness, vomiting, marked distention. Seemingly a typical picture of peritonitis, therefore laparotomy.

Intestinal loops greatly distended, covered with fibrin. Between them large amount of brown-greenish pus. In right flank, along ascending colon reaching up to liver, a large mass. Uterus large and soft. Thickened tubes a fiery red, apparently not containing any pus. Under guidance of a forceps, pushed up through the vagina, posterior fornix and peritoneum are opened and gauze strips from above drawn into vagina. Gauze strips are placed from abdominal incision into both flanks and the vesicouterine space. Before closing abdominal wall in three layers one liter of Merck's coal emulsion is introduced. Pus shows streptococci.

Wound heals in part *per secundam intentionem* otherwise entirely satisfactory convalescence.

Discharged cured on March 28, 1914.

This was a case of peritonitis observed at its very beginning and during its further progress, therefore, it became possible to perform the laparotomy at the proper time. Operation was limited to the minimum, namely drainage without removal of any organ.

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S. N., thirty-two years old. Admitted Jan. 29, 1916, discharged cured March 13, 1916.

*History.*—Early in January an abortion. Curettage. Then some fever and pain, which gradually disappeared within next 14 days under conservative treatment. For past three days again pain all over abdomen.

*Stat. pres.*—Icteric discoloration of skin and sclerae. Temp. 38.6° C., pulse 200. Tongue moist, only slightly coated. Very frequent respiration. Abdomen is rigid, somewhat distended and very tender approximately up to level of navel. Above navel abdomen is flaccid, and only slightly sensitive to pressure. Fetid vaginal discharge. Uterus enlarged, dextroposed, soft.

Within the next few days icterus becomes more marked, but pulse falls to 140. Tenderness of lower abdomen remains unchanged. Repeated vomiting. Upper soft abdomen clearly



separated from tender and distended lower portion by a distinct groove. Therefore we refrain from operation which would seem indicated by the other threatening symptoms. (The final outcome proved the correctness of this decision.)

With the groove, running transversely across the abdomen, becoming more and more distinct, the peritonitis actually localizes itself strictly to the pelvis.

Without any operative interference patient recovered and was discharged in good condition on March 13, 1916.

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E. W., forty-three years old. Admitted May 22, 1916, discharged cured July 29, 1916.

*History.*—On May 8, spontaneous partus. On ninth puerperal day patient got out of bed in spite of slight abdominal pain. On May 21, intense abdominal pain, fever, vomiting, chills.

*Stat. pres.*—Temp. 39.7° C., pulse 120. Fast respiration.

Abdomen distended approximately up to navel and very tender. Purulent discharge. Cervix closed. Uterine fundus not distinctly palpable on account of meteorism.

May 23. Patient looks worse. Both tenderness and distention reach to two fingers above navel. Upper abdomen soft and not tender. Temperature continues high, pulse 144. Enema followed by escape of stool and gas.

Next two days condition unchanged. Enema effective. Vomiting continues.

May 25. In front of uterus a resistant mass; at its upper margin near navel a furrow visible.

May 27. This furrow more marked. Most obvious difference in the portions of abdomen above and below this groove.

June 2. Tenderness and tension reaches only to one finger below navel.

Next a bilateral parametric infiltration becomes evident, which under conservative therapy is gradually resorbed. Rises of temperature up to 39.8° C. occur with diminishing frequency, and gradually temperature sinks to normal.

Patient discharged perfectly well, on July 29, 1916.

Aggravation of all the symptoms of peritonitis and a rising pulse rate beyond doubt seemed to call for operative interference in this case. Only the transverse furrow, gradually increasing in depth, induced us to wait. The outcome fully justifies our attitude. Patient was saved an operation. It seems very probable that the laparotomy might have changed the localized into a general peritonitis.

H. A., admitted June 13, 1916, discharged cured Aug. 4, 1916.

*History.*—On May 26, spontaneous delivery. Since June 8 fever, abdominal pain, vomiting. Stool and gas passing normally.

*Stat. pres.*—Temp. 39.2° C., pulse 120. Examination of lungs and heart negative.

Abdomen slightly distended and tender, especially in lower part. Upper abdomen soft and not tender.

June 15. Nausea but no vomiting. Distention now extending up to navel, very sensitive. Upper abdomen soft.

June 16. Condition practically unchanged, though distention and tenderness below navel possibly more marked, making more evident the difference with upper abdomen. Vomited once.

June 17. Excessive meteorism of lower abdomen with intense pain. At the level of navel a distinct transverse groove visible, below it abdomen is distended, above it, it is flat. For this reason no operation.

For the next few days condition remained practically stationary. Pain and meteorism persisted but some stool with gas was evacuated by means of enemas.

During the following weeks the peritoneal symptoms gradually subsided. Infiltration formed first in left and later also in right parametrium.

Patient discharged well on Aug. 4, 1916.

Abdominal findings, pulse and pain should have induced us to open the abdomen promptly in accord with our general rules in view of the diagnosed peritonitis. Experience gained in the meantime in regard to the favorable prognosis in cases which develop such a groove, induced us to proceed conservatively. The result justified us.

These last three cases are cited only as good illustrations out of a number of similar observations.

### Ligation of Veins

The third type of operation employed in the surgical treatment of puerperal infection consists in the ligation of veins.

The operation had been suggested first by surgeons for the purpose of preventing the entrance of detached particles of a necrotic thrombus into the circulatory system.

The first attempt in this direction was made by Lee in 1865. He ligated the cephalic vein in a patient with an infected injury of the hand when she began to have chills. In the war of 1870 Fischer tried the procedure in several cases but without result. In 1877, Kraussold extirpated a part of the thrombosed femoral vein in a patient who exhibited the symptoms of a pyemia subsequent to a thigh amputation. Later this idea was propagated by otologic surgeons. Zaufal, in 1884, ligated the jugular vein in a patient with a thrombosis of the transversal sinus. Today ligation of veins is extensively practiced by otologists.

Priority for vein ligation in the therapy of puerperal infections can be justly claimed by Sippel, who proclaimed its theoretical benefit although he had no opportunity actually to perform the operation. The first ligation of the spermatic vein, without effect, was done by W. A. Freund in 1896.

Credit for the first successful ligation in a case of puerperal infection is generally accorded to Trendelenburg who in 1902, after several failures, finally succeeded in saving a patient by ligating the hypogastric veins.

Since that time the method has found favor in various countries, in Austria and Germany having its chief advocates in Bumm, Leopold, Veit and Latzko. They have employed it with varying success in many cases and spent much effort in promulgating the operation in their writings.

For reasons, which I shall give presently, we had but little opportunity to acquire personal experience with this operation.

**Technic of Operation.**—Most commonly, approach to the veins to be ligated is gained from above. Only a few operators have shown preference for the vaginal route. In regard to the abdominal route, two opposing views are held. Trendelenburg favors an extraperitoneal operation

while Bumm employs the customary transperitoneal laparotomy. Trendelenburg makes the incision parallel to Poupart's ligament through skin, fat, fascia and muscle layers and then bluntly pushes the peritoneum off until he reaches the hypogastric veins. An upward extension of the incision permits one to reach the spermatic vein in a similar manner. Bumm makes a midline celiotomy and searches for the vessels after having split the posterior peritoneum.

The reduced risk of starting a general peritonitis, which must be granted Trendelenburg's method, is minimized by the difficulty, if not impossibility, of good exposure with it, and by the fact that through one incision the veins only of one side can be reached. Bumm's method exposes the entire system of genital veins up to the vena renalis or cava, on both sides, and therefore, in principle, is more advantageous.

Only a few operators have followed the advice of Taylor and of Latzko, who ligate or resect the veins above the exudate reached through a vaginal incision. The method hardly deserves support because the operative field is narrow, exposure most unsatisfactory and the possibility of ligating larger veins decidedly limited. There are added the extreme difficulty in technic and the danger of severe hemorrhage.

As in all the other operations, here also we meet with the three important and difficult questions: In which cases shall ligation be done, at what time, and in which form?

Again it will prove practically impossible to supply definite answers however desirable that may be, because final decision in every case necessarily must depend upon the personal judgment of the operator, and because in the estimation of the ultimate results the *propter hoc* cannot always be precisely differentiated from the mere *post hoc*.

In regard to the first two questions, which are better dis-



cussed conjointly, I can quote Vauverts and Paucot, who accumulated their experience on 82 operations of this sort. They consider vasoligation indicated in cases in which an exacerbation is observed after several previous remissions. They accept, however, a periphlebitis as just as strict a contraindication against operation as metastases. According to Michels only those cases offer hope for success which do not take an absolutely acute course. He bases this attitude on the assumption that in them the germs are of restricted virulence so that the wall of the vein offers sufficient protection against their invasion into adjoining tissues. Relative comfort and good pulse in the interval between chills indicate to him that this is the proper time for the operation. Seitz operates in all pure cases of thrombophlebitis which show no signs of a lymphangeitis, even if there are slight pulmonary complications. Bumm proceeds with ligation in subacute or chronic cases when the fact is established that there is a purulent thrombophlebitis. Beuttner goes further and considers ligation indicated in every clear instance of pyemia.

Veit and Leopold thought that the suitable time for surgical interference is at hand after the second or third chill, Trendelenburg right after the first. Von Herff is willing to wait until after the fifth or sixth chill but evaluates as chill any rapid rise and rapid fall of temperature. Latzko also is unwilling to wait too long and operates if the patient has a continuously high temperature with an occasional chill and when her general condition appears unsatisfactory. Nyulasy favors early operation.

Guiccardi insists that ligation should not be considered simply as a last resort. Similarly Bumm confesses that he has ligated veins in some patients as a prophylactic measure when fever and a septic infection of the cervix had been ascertained during labor, especially if a major operation



had been required for delivery and extensive injuries were unavoidable.

Doederlein and Warnekros feel that ligation should be performed only if the temperature curve shows sharp remissions with chills in long intervals late in the puerperium.

It thus seems that very few gynecologists operate in acute cases but that most of them regard ligation as justified only in subacute or chronic cases and even then only under certain limitations, a view seemingly fully shared by American gynecologists.

The blood culture plays an unimportant rôle in the decision, because even a positive culture is not looked upon as a contraindication. The general condition and pulse really are the only deciding factors.

There is but little disagreement concerning the method of operation. As already stated, outside of Trendelenburg only a few, e.g., Veit, choose the extraperitoneal approach, the latter especially if the infection has spread into the tissues surrounding the affected veins, a point also made by Halban as early as 1907. Bumm is willing to resort to the extraperitoneal procedure if the process certainly is limited to only one side, or when the exact location of the thrombus can be determined beforehand. Of late Martens again defended this route.

There exists no definite agreement concerning the most favorable site of the ligation. Formerly as a rule only the hypogastric and spermatic veins were ligated. Failures led to further investigations and it was observed that very frequently the thrombosis will extend much higher or might have occurred in anomalous vessels so that the customary ligation was obviously insufficient. Great credit must be given especially to Kownatzki for such anatomic studies. They are directly responsible for the present better understanding of conditions and for newer methods of

operation. He found that the veins of the uterus and of the bladder join to form the *vena iliaca media*, which unites with the *iliaca interna*, that brings the venous blood from the gluteal and rectal regions. These combined, as *vena hypogastrica*, empty into the *iliaca communis*. Since there is a possibility that this last union is missing, the likelihood of a deficient effect of the ligation of but one of the two stems is apparent. Ligation of the *hypogastrica* in the presence of such an anomaly would still permit the *media* to carry the blood from the uterus into the *communis*. These findings actually induced Bumm to discontinue ligation of the hypogastric vein in favor of ligation of the *iliaca communis*, especially if the thrombotic process is limited to one side. For this same reason ligation of the *communis* was adopted as well by Vauverts and Paucot, and also by Beuttner, who thought that in this way furthermore, all the branches of the *vena obturatoria* are controlled.

At first the objection was raised that ligation of the common iliac may result in gangrene of an extremity. Extensive experience has, however, completely dissipated such fear. In chronic cases both common iliacs can be tied since the long-continued thrombosis necessarily has led to an entirely sufficient collateral circulation. In some cases of this sort even the *vena cava inferior* has been ligated without any alarming signs of disturbed circulation.

As the result of all these investigations and observations today practically all operators ligate the common iliac at least on one side and regard ligation merely of hypogastric and spermatic veins as entirely valueless. A very thorough discussion of the problem in all its aspects and a careful consideration of the extensive literature will be found in Wormser's comprehensive survey, prepared for the Congress of Gynecologists in Strassburg (1909) and in the exhaustive monograph of Venus, published in 1911.

While in Europe in general the view prevails that ligation or excision respectively should be limited to the affected vessel area, a number of American writers (Baldwin, Hirst, Jellet, Wilson, Yates, etc.) think that especially in cases of extensive thrombosis, it is preferable to perform a hysterectomy at the same time. Baldwin in particular claims that in this manner through better drainage the operative results are greatly improved. While according to Miller, of 188 patients on whom ligation was done 108 died, a mortality of approximately 58 per cent, Baldwin saw of 67 patients, operated with the addition of a total hysterectomy, 47 recover, which means a mortality only of 30 per cent. However, we see that, e.g., Clark, an adversary of all operation for these cases, likewise objects to this procedure.

There exists some discrepancy of views as to whether it is preferable simply to ligate the vein or to combine ligation either with clearing out of the thrombus or entire excision of the thrombosed portion of the vessel.

The deciding factor is whether or not the thrombus is suppurated. If suppurated one could dare to open the vessel wall only if the operation was done by the extraperitoneal route. Proper drainage might preclude further extension of the infection, which would be impossible with a transperitoneal operation. Therefore, in the latter operation it will prove advantageous to refrain from removal of the thrombus or vessel resection, and still better, to refrain from any attempt to even dissect out the thrombosed veins. It is just this possible risk of spread of the infection which minimizes the total effect of this operation. Before, and often during operation it is impossible to determine whether the thrombus contains pus or whether a periphlebitis has set in. Therefore, not rarely after having opened the abdomen one is forced by unexpected findings to close it with the definite knowledge that no good but probably

some harm has been done to the patient. Thus one might later be forced to operate once more, this time by the extra-peritoneal route.

**Indications for operation.**—While we admit that we have gained very little personal experience with the ligation of veins, we feel that certain observations at the postmortem table and theoretical considerations entitle us to express an opinion concerning its assumed value.

There is first of all this difficulty of determining definitely in a case of puerperal fever, that we are dealing with a hematogenic infection. Some writers, among whom I can mention Bumm, Lenhartz, Trendelenburg or Latzko, claim that they can make the diagnosis under certain conditions. The temperature curve is supposed to be characteristic, since several chills a day distinctly indicate the repeated establishment of metastases from emboli detached from the infected thrombus. This might be true for some cases but certainly does not represent a general rule. We have carefully studied at autopsy cases with just such temperature curves and found that the infection was of a strictly lymphogenic type.

Our statistics, based on 163 necropsies, show the following facts:

Out of 82 cases, in which vessels were involved, only in 47 (57.3 per cent) were chills recorded, or in other words, in practically one half of them they were missing.

Out of 81 cases, in which the vessels were not involved, in more than one quarter, exactly in 22 (27.1 per cent) chills had occurred.

Several chills were observed: in 25 per cent of hematogenic and in 10.14 per cent of lymphogenic infections.

One can therefore deduce that chills occur in the hematogenic type infection of puerperal fever approximately twice as often as in the lymphogenic, furthermore, that certainly not all hematogenic infections are leading to chills. If a



patient has chills, a hematogenic infection probably exists, absence of chills does not exclude the possibility of its presence.

For this reason it is unjustifiable to determine the indication for ligation of veins on the mere fact that the patient has chills or had several chills, as is done, e.g., by Leopold, v. Herff, Trendelenburg. Ligation obviously is an operation of possible value solely in the hematogenic type in which however, chills might be absent. Presence of chills in cases of the lymphogenic type or in the combination of both types under this rule would lead to useless operations. Every chill might be the last, but, of course, the very first chill might also have indicated the transport of a sufficient amount of infectious material into the general system to minimize if not completely annihilate any possible effect of a vasoligation.

The undeniably correct observation that pulmonary metastatic abscesses are incomparably more frequent in hematogenic infection can hardly be utilized for a definite diagnosis because in autopsies we have found this pulmonary complication not so rarely in cases of the lymphogenic form also. However, so serious a complication probably should be accepted by itself as a strict contra-indication against any operation.

Bacteriologic blood studies offer no clue concerning the route over which the infection is entering the general system because both in the hematogenic and the lymphogenic types, blood cultures may be positive or negative.

Of not greater diagnostic value is the presence or absence of a septic endometritis. Theoretically one might assume that there is less likelihood of an endometritis if an infection seemingly spreads along the veins. Our pathologic-anatomic investigations showed the endometrium free from any pathologic change in 19.3 per cent of hematogenic, and 17.4 per cent of lymphogenic infections, not sufficient dif-



ference to allow any deductions concerning the type of infection in the individual case.

The only certain evidence for a hematogenic infection is the palpation of wormlike, thrombosed vessels in the areas of the spermatic or hypogastric veins respectively. We have been able to base in a number of patients the precise diagnosis of septic thrombophlebitis on such palpatory findings, but unfortunately even then one is unable to say how far upward the thrombotic process extends. But it is just this point which determines the feasibility of a ligation. Another difficulty, likely to annul the value of positive palpatory findings, is offered by the fact that there might exist outside this hematogenic also a lymphogenic infection, and this combination we have often ascertained in our material. To ligate veins in a case of this sort is not only a fruitless procedure, but distinctly harmful. If the thrombosed vein is embedded in edematous tissue and the lymphangitis deep-seated, neither inspection nor palpation during operation will permit its definite diagnosis.

Some authors claim that they have palpated thrombosed spermatic veins through thin abdominal walls. While we confess that we have never been able to do this, we deny that even this finding is of distinct merit since it does not decide the essential question whether the thrombosis is not already extending into the renal veins or still higher up.

Such uncertainties, especially in regard to the extent of the process, necessarily diminish greatly the possibility of establishing precisely the existing justification for ligation.

What advantage would it be to palpate thrombosed veins on the one side without any information as to whether possibly vessels much further up on the other side were already involved? This one fact alone can only confirm one's opinion concerning the impracticability of the extraperitoneal method of operation. A routine bilateral extraperitoneal operation might be theoretically conceivable, but in prac-

tice beyond doubt would do great harm to many patients. What is gained by the palpation of affected veins as long as we cannot at the same time exclude a coexisting lymphangitis and are absolutely ignorant as to whether pus might already be traveling through the tubes toward the peritoneal cavity? Progress of the infection by way of the lymph channels leads only comparatively late to a parametritis or an ovarian abscess, while pus passing through the tubes relatively early sets up a pelveoperitonitis or a pyosalpinx. But all these significant features of the infectious process might become unrecognizable in a really foudroyant case.

How important it is to take into consideration all these facts might be seen from certain postmortem findings: Out of 163 necropsies, 46 (29.22 per cent) showed a combined hematogenic and lymphogenic propagation of the infection, while only 36 (22.08 per cent) represented the purely hematogenic type.

As long as we cannot positively exclude a concomitant lymphangitis, I repeat, a clear indication cannot be established for ligation, an operation which imposes considerable risk on the already very sick patient. We must remember that we cannot be certain that we shall be able to make this diagnosis even with the opened abdomen before us and that if we make the diagnosis we shall have to desist from the contemplated ligation and close the abdomen.

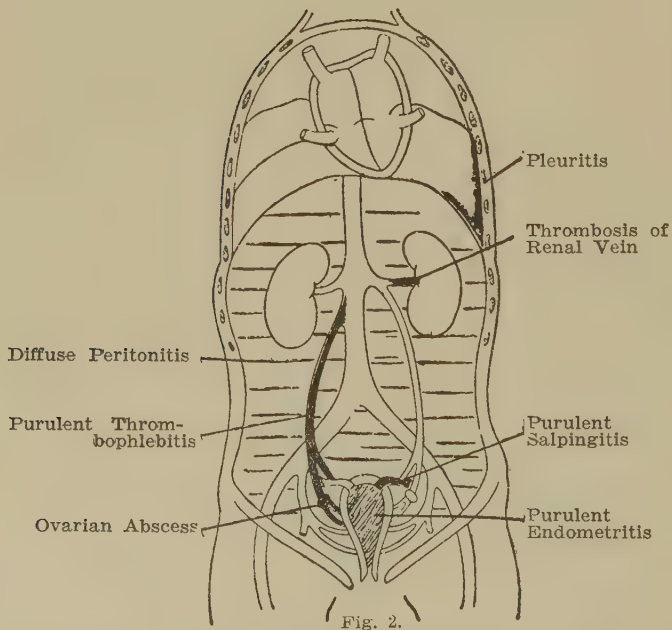
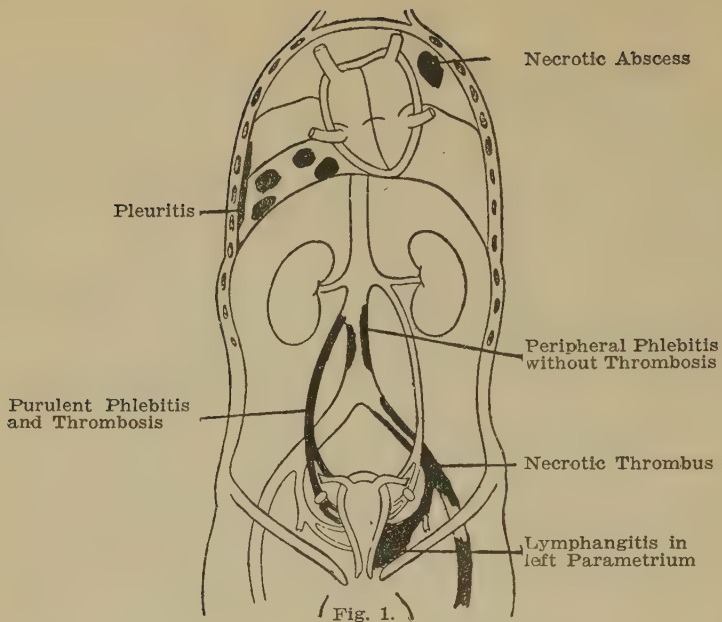
Granted we find the vessel thrombosed as expected, are able to follow the thrombus to its seeming end and to place a ligature there, we still remain entirely in the dark whether possibly a part of the vein higher up already is infected or in a state of beginning thrombosis, whether presently somewhere else another thrombus will form, equally as dangerous to the patient as the one presumably just rendered innocuous. I say "presumably" because as

a matter of fact the ligated thrombus continues to be a potential source of further trouble. The ligation certainly temporarily prevents the detachment of an embolus but the focus is retained and from it the infection might proceed to spread now by way of the lymph channels.

Ligation obviously cannot preclude the possibility of a thrombosis in other veins since it is impossible even by the most radical type of operation to isolate the genitalia completely from the circulatory system. Furthermore, there always is a chance that the process will extend in a central direction from any ligated vein. It might be technically possible to ligate or extirpate the thrombosed veins, but quite naturally the outlook will be very unfavorable whenever many veins are involved or when the process is found to have reached the vena cava or the left renal vein. The vena cava has been successfully ligated in a few cases but the ligature must unavoidably be placed below the entrance of the renal veins. Therefore also cava ligation cannot always secure sure protection if the left spermatic vein is not separately tied.

There is still another point which in my opinion has not been sufficiently stressed in literature. We saw at autopsy, cases in which e.g., (as illustrated in Fig. 1) the right spermatic vein and the left common iliac were thrombosed with a coincident purulent phlebitis along the wall of the cava but without its thrombosis (therefore it could have not been diagnosed by palpation). In another case (Fig. 2) the spermatic vein on the right side and the renal vein on the left side contained a thrombus.

Such instances of "discontinuous thrombosis," as we call them, are entirely unsuitable for ligation since unquestionably the ligature would be placed only on the peripheral vessel while the more centrally located thrombosis most likely would be overlooked. The operation would have



"Discontinuous" Thrombosis. (From Halban-Koehler: Pathologische Anatomie des Puerperalprozesses, etc., Vienna, 1919.)

proved useless and the process would have proceeded from the other focus without interference.

Another factor of far-reaching importance in this problem is the complication of a thrombosis with a phlebitis or periphlebitis. The relative frequency of this latter combination is likewise established by our autopsy findings. Out of 82 cases we found in 15 (18.29 per cent), that is, in one out of every five, a periphlebitis.

In regard to this concomitant phlebitis, it is not yet certain what represents the primary factor, whether the phlebitis causes the thrombosis or the thrombosis leads to the affection of the vessel wall. But either way, for the problem of ligation it is significant that mere ligation would not check the pathologic process within the vessel wall. The infected thrombus remains in place and some of the *vasa vasorum* or lymph vessels within the vessel wall might carry the infection further on. Resection of the thrombosed vein in this respect likewise cannot prove a reliable preventive since with the existence of a phlebitis the process really has become one involving the lymph-system, and the continuity of the lymph vessels is not necessarily interrupted even by the excision of a portion of the vein.

Decidedly unjustified is the assumption of Friedemann that in the further progress of the thrombotic process primarily an aseptic thrombus forms whose secondary infection is prevented by the ligation. Theoretically one might think that a thrombus at first is aseptic if actually the result of an existing pathologic alteration of the vessel wall, but we do not know of a "germ proof" ligation and even such a ligature could not interfere with the prompt invasion of the thrombus by bacteria from the admittedly infected vessel wall.

Thus we arrive at the inevitable conclusion that neither ligation nor resection represent reliable means of checking



and localizing a thrombotic process or of saving a seriously sick patient even if her infection is of the purely hematogenic type.

The difficulty of diagnosis and the impossibility of differentiation between mere thrombosis and beginning suppuration express themselves in the dilemma of choosing the appropriate operation in the individual case. Considering all the elements of uncertainty especially in regard to supuration, one would be forced to decide always in favor of Trendelenburg's extraperitoneal route because a laparotomy on the whole offers less certainty of accomplishing the aim in view.

As early as 1907, Halban pointed out that meeting unexpectedly during a contemplated ligation with a thrombus in the state of suppuration, one should necessarily be forced to deal with it in accord with well established principles of the treatment of abscesses or phlegmonous processes, that is, to open and drain it. If approach to the suppurating thrombus were gained through a laparotomy incision one would face a most reprehensible task because with dissection of such a thrombus and the escape of pus from it a secure protection of the adjacent tissues against infection would be a certain impossibility. Therefore, one should as a matter of dire necessity always do the extraperitoneal operation in spite of its obvious shortcoming, namely that still another operation on the other side will very likely be required. This will inevitably in every case raise the serious question whether the patient's general condition allows a double or two separate operations of such extent.

The transperitoneal operation in comparison is a shorter and easier procedure of less severity, but one distinguished by its definite limitations. So whatever decision one makes one has to choose between great danger to the intact peritoneum on the one hand, and a long operation, on the other hand, which might later have to be repeated on the other

side if their simultaneous performance appears too hazardous.

In doing a vasoligation the one essential fact must be kept in mind: The purpose is accomplished only if the ligature has with certainty been placed well above the thrombus—and not through the thrombus as is not rarely done. Martens, e.g., reports that in one of his cases the stoppage in the cava had extended so far up that the ligature unavoidably had to be placed within the area of thrombosis. Peculiarly enough this patient, continuing with chills for another forty-three hours, finally recovered.

Those who have studied necropsy findings carefully, as we have done, can never expect very much from this operation. They have seen too often how quickly secondary thrombotic processes may have started in lungs, kidneys or endocardium and how frequently there exists a combination of thromboses in venous plexuses so far apart that the aforementioned essential condition for placing the ligature properly cannot be met.

If some of these operated patients actually recover, obviously the proof is still lacking that they were saved by the interference.

To be sure some authors record remarkable results, e.g., Veit, 6 recoveries in 20 ligated cases; Latkzo, 10 in 28 operations; Miller, 80 in 188 cases; Baldwin, 47 in 67 ligations with simultaneous hysterectomy. Venus in a collection of 115 ligated cases reported in literature calculated a mortality of 66 per cent which seems low in comparison with the mortality figures given by Winkel as 83 per cent, Baldwin as 100 per cent or by Bumm as 100 per cent in acute cases and 83 per cent in chronic cases. But, on the other hand, there is Olshausen claiming only 39 per cent, and Opitz between 30 and 40 per cent of mortality with a strictly conservative treatment. A comparison of all these

figures carries no conclusive assurance that all the good results were necessarily dependent upon operation.

Every experienced obstetrician will readily recall cases in which the clinical symptoms were such that he felt greatly inclined to resort to this operation. Then the operation for various reasons could not be performed, or the chills suddenly ceased, and the patient recovered under conservative treatment. If in such a case the ligation actually had been done, the recovery undeniably would be gladly credited to it.

We all know of spontaneous recoveries after many chills and I well remember one patient with more than a hundred of them. An operation on her certainly would have served as a splendid advertisement for the marvelous efficacy of ligation.

The advocates of this procedure claim that its beneficial effect is evidenced by the immediate cessation of chills and its failure by their continuation. This criterion does not seem reliable. As already mentioned we are not so rarely surprised by the sudden stopping of the chills, while on the other hand, in the reports of some of the cases recorded in literature as cured by ligation, the fact is definitely mentioned that there occurred one or more chills subsequent to the operation. We can never positively substantiate the assertion that ligation really has saved this or the other patient and that she would have died without fail if she had not been operated upon. The case of Martens, referred to above, in this respect is most instructive, and properly interpreted rings the death knell of this procedure. The thrombus was excessively long; the ligature could not possibly have been beneficial to the patient because it was placed in the midst of the affected area. The only possible effect from it one could think of would be that it cut the thrombus in two and therefore indeed favored detachment of particles from its upper portion.

Thus one experiences great difficulty in accepting Martens' explanation of the subsequent recovery as due to the "elimination of the larger portion of infectious material" by the ligature. As in all instances of puerperal sepsis we are dealing in a case of this sort not with a definite quantity of toxic material but with an ever-regenerating source of toxic substances. It might also be pointed out that Martens' patient after the operation had more chills, therefore, personally I have no doubt that this is one of those instances in which the patient recovered not so much as the result of, as in spite of the operation.

Vasoligation, first accepted with exalted hope at least for theoretical reasons, as a matter of fact has not fulfilled the expectations of the gynecologists. Neither clinical experience nor pathologic-anatomic studies have ever let us regret that we have resorted to ligation or resection not more often, nor do we feel that we have been negligent in our duties in any individual case for not having operated. Experience and studies had prevented us from ever gaining an unjustifiedly high opinion in regard to the possible efficacy of the operation. We realized that its possible usefulness is unavoidably restricted by difficulties of diagnosis and by such insurmountable obstacles as extensive or discontinued thrombosis. I emphasize that practice, critique and investigations together account for our evident pessimism because Martens specifically states that "the adverse attitude of Halban and Koehler seems unjustified since their opinion in the main is based upon severe alterations discovered at autopsy." They did not form the sole basis of our views, but we admit they strongly convinced us of that uselessness of ligation which was suggested to us by a critical study of the reports in literature and by painstaking clinical observation of every one of our cases. It is for this reason that as a matter of fact in our rich material we executed a ligation in but one case. The operation was



quickly done and there seemed to be an immediate improvement but it lasted only a short time and the patient finally succumbed to the infection. It would be impossible to deny that the patient's chances under conservative treatment might have been better. We have never felt inclined to try another ligation.

S. L., twenty-eight years old. Admitted May 27 1915, died June 15 1915.

*History.*—Delivered spontaneously on May 19. Patient got out of bed on the third day postpartum. Since then pain in lower abdomen, fever and several chills.

*Stat. pres.*—Temp. 39.9° C. Slight vaginal hemorrhage. Uterus poorly involuted. Fundus midway between symphysis and navel. Adnexa not involved.

During the next few days one or more chills daily, temperature rising to 40.8° C.

June 8. Intravenous injection of coli-vaccine (100 million bacteria).

No effect on temperature or general condition. Bacteriologic findings of blood remain unchanged; repeated positive blood cultures with pure growth of streptococcus.

Coli-vaccine injection repeated twice, also without effect. Temperature remains high. Chills daily.

Since palpatory findings continue to be negative and nothing abnormal can be found in lungs, kidneys or heart, we finally decided to try ligation after patient had 34 chills in all. Laparotomy. Careful investigation reveals that only the right spermatic vein is thrombosed almost to its upper end. Cava free. Peritoneum is split over the affected vein, the latter is ligated at its distal and proximal end and excised.

Approximately two hours after operation another chill, which was the last up to death which occurred eight days later, but during all this time temperature remained high, often reaching 40.0° C.

It is our first and only case in which we gave ligation a trial. Why we tried it in this instance and why we never repeated the experiment, I trust, has been fully explained in the preceding pages.



## CHAPTER VI

### MEDICINAL TREATMENT OF THE GENERAL INFECTION

#### **Antiseptics**

The foregoing chapters have revealed the fact that not too much can be expected from the surgical treatment of puerperal infections. If improvement or recovery follows the operation either can but rarely be definitely credited to the interference.

The innumerable nonoperative methods of therapy which have been proposed unfortunately offer no more certainty concerning a beneficial effect, but at least, as compared with operative methods, they possess the distinct advantage of implying less immediate risk to the patient. They always leave the opportunity to make a trial with still another form of conservative therapy if the failure of the one becomes apparent. Also such change will not necessarily harm the patient.

The knowledge that fever of the puerperal woman is the product of an extension of the infection into the general system, logically led to efforts at combating the systemic intoxication by reducing the virulency of, or destroying the responsible microorganisms through introduction into the blood of certain antiseptics, which usually are applied only externally. In accord with this idea we find records of trials ranging from bichloride the strongest, down to the weakest of bactericides. A simple consideration, however, forces the conclusion that reliable curative effect could not be expected from any one of them and that a favorable outcome after their use often might be solely a fortunate coin-

vidence. Doses that can be administered intravenously without undue danger, necessarily are so minimal that one could not hope to obtain their presence in the blood in a concentration sufficient to be effective. The maximal intravenous dosage for bichloride e.g. is 5 mg. which would represent a final dilution in the blood stream of 1 to 1,000,000. Even if certain laboratory experiments establish the efficacy of such remedies, for their practical application this proof means next to nothing. As I have already pointed out, the experiment in the test tube bears no resemblance to processes and conditions existing in the body and especially in the diseased body. In the experiment we work with a potent disinfectant which acts directly on the bacteria. In practice we deal with the same disinfectant to be sure, but in greatly diminished concentration. Furthermore, the greater part of the injected antiseptic immediately is bound up to the protein of the body cells, and indeed only a small part of it remains to take up the fight against the invading bacteria. In the experiment the antiseptic has free access to the bacterial growths on the culture medium, while in the patient it can reach only with difficulty bacteria lying well sheltered, and not at all those which are in tissues that are not touched by the circulating blood, as, e.g., those in the midst of a thrombus or deep in the endometrium.

Even granted that all these obstacles to access could be removed, and conditions in the patient then would resemble closer those prevailing in the test tube, therapeutic failure still is likely to result because of the fact, well known, that the normal body cell is more sensitive than the bacterium covered by its protective cover, so that the body cell more likely than the bacterium will be destroyed by the disinfectant. In spite of many strides that have been made in this direction, we are as yet unfamiliar with that ideal antiseptic in which a bacteriotropic greatly outweighs its natural organotropic affinity.

Medicinal curative methods based on the introduction of antiseptics into the blood stream have so far proved inefficient.

**Bichloride.**—The first attempt to disinfect the entire body in a case of general sepsis was made by Bacelli (in 1894) with bichloride. With great zeal it was tested in Italy but never generally approved. Several years later this method was resurrected from deserved oblivion by Hungarian gynecologists (Barsony, Kenezy). They became quite enthusiastic after extensive trial on a large material and emphasized in particular its value as a prophylactic. As a rule from 1 to 5 mg. of a pure sublimate preparation were injected intravenously. Only Soligoux used it intramuscularly. Abadie preferred the mercuric cyanide. As contraindications were accepted: diarrhea, tenesmus and renal lesions. Many other writers, however, denied the method any merit.

The rationale of the bichloride treatment was explained on the basis of certain experiments on animals. Mariani, e.g., claimed to have observed very satisfactory experimental results, both prophylactic and curative, ascribed to an augmented resistance in artificial infections with streptococcus and anthrax. He thought that bichloride injected into the blood proved less potent as a bactericide (as one might have expected!) than as an antitoxic. The agglutinating power of the blood serum was found to be increased with doses of 1/50 of a mg. per one kg. body weight.

Kalledey also ascertained an increase of the protective substances in the blood following their primary reduction. Theoretical considerations led other writers to explain the effect of intravenous bichloride administration on the basis of an antitoxic, leucotactic or virulence-reducing ability. Polizotti speaks of an increased opsonic index.

We have no personal experience with sublimate treatment. Theoretical objections and lack of confidence both

contractions and thus prevent the common subinvolution. A well contracted uterus is more apt to obstruct or at least to delay the ingress of more infectious material into the circulatory system.

In the few cases treated in this manner we observed no results. Since our expectation was not exaggerated, the disappointment was not great. But we did not hesitate to give large doses up to one gm. three times a day until tinnitus or other disagreeable symptoms appeared. Only rarely was the intravenous administration followed by a minimal fall of the temperature which we disregarded. Occasionally the leucocytes increased in number, but only temporarily.

Newer preparations of quinine, optochin<sup>1</sup>, vuzin<sup>2</sup> and eukupin<sup>3</sup>, we have so far not used extensively enough to form a personal opinion. Theoretically they seem rather promising. They exhibit a high bactericidal power in the test tube even to streptococci, they proved very effective as external antiseptics during the war and they yield gratifying results within the blood stream, at least in the treatment of malaria. In cases of puerperal fever so far they have not shown any superiority over the other antiseptics. Their failure, like that of other antiseptics, is probably due to the fact, peculiar to puerperal infection, that there exists a conspicuous tendency for thrombi to form. The interior of these clots remains inaccessible to the antiseptics. They are prevented from exerting their effect just where it is most needed. Only further observations on a larger number of cases will offer any information concerning the value

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<sup>1</sup>Ethylhydrocuprein. A white powder, easily dissolved in water. Optochinum hydrochloricum has the same qualities. Originally used for pneumococcus infections in doses of 0.2 to 0.25 gm. for adults. Very unfortunate sequelae, such as vomiting, deafness, visual disturbances, in some instances leading to permanent blindness, make it desirable to use the less soluble optochinum basicum in the same dosage.

<sup>2</sup>See footnote<sup>3</sup> on page 76.

<sup>3</sup>Isoamylhydrocuprein. A white powder, soluble in fats. Eucupinum bihydrochloricum is easily dissolved in water. In effect and also in regard to sequelae the substance is very similar to vuzin.



of these new quinine derivates in the treatment of a complicating peritonitis.

It is possible that in the limited number in which we have tried these quinine derivates we have made use of too small doses. We never studied them systematically. Many of the cases had been treated in other ways before admission to the hospital and this by itself always precludes the reliable valuation of the effect of a drug.

S. H., thirty-six years old. Admitted Aug. 28, 1916, died Sept. 28, 1916.

*History.*—Last menses middle of April. For past few days vaginal hemorrhage, fever. Small pieces passing from uterus.

*Stat. pres.*—Slight genital hemorrhage. Uterus anteverted, soft, somewhat enlarged. Adnexa free. Temp. 39.2.

Blood culture: Streptococci, slight hemolysis.

Aug. 31. Temperature continuously high. Intramuscular injection of milk (10 c.c.) In the evening temperature up to 40.2°, but no chill. In next days, with temperature continuing high, gradually infiltration of both lower lobes of lungs developed. Patient was given by mouth three doses of optochin (0.25 gm.)

No effect of this drug either on pulmonary or general condition can be noticed. Pneumonic infiltration remains unchanged.

September 28. Patient dies from pneumonia and a complicating pericarditis.

In view of certain relations between the pneumococcus and the streptococcus it could have been expected that optochin, presumably so effective in pneumonia, might be of some value in sepsis. Unfortunately the great toxicity of the substance precludes a dose which would seem sufficient for a systemic septic condition. For this reason we administered optochin only in a few cases, always without noticeable benefit. However, these cases really are not conclusive because invariably we gave other remedies simultaneously.

**Magnesium Sulphate** has been warmly recommended by Harrar, and Huggins (in 1 to 2 per cent solution with a total dose of about one gram per day). The solution must be freshly prepared in distilled water and is sterilized in



the autoclave. The injection is made very slowly since otherwise dyspnea may be observed. Given with these precautions the substance can do no harm, causes neither hemolysis nor globulin coagulation. The few recorded good results are not very convincing because most if not all of the benefit probably more properly should be ascribed to the infused fluid.

**Silver Nitrate.**—In this connection I shall mention the suggestion of Ilkewitsch to infuse intravenously 500 c.c. of a silver nitrate solution (1:8,000 down to 1:20,000) and of Humes, who also employed a diluted silver solution.

**Formaldehyde Preparations.**—Most extraordinary results with formalin infusions were reported by Barrow in 1903 before the New York Obstetrical Society. Of eight patients treated in this manner only two died. Each received a 1:5000 solution in a first dose of 500 and a second of 750 c.c. The rejection of the method was practically unanimous. The chief argument finally raised against formalin was the fact that in comparative series identical results were recorded from saline infusions (Marx, Brodhead, Vineberg, Dudley, Pryor, Waitzfeld).

Experiments made with intravenous formalin injections on animals furthermore failed to furnish any theoretical basis for its assumed usefulness. Most of the investigators ascertained that small nontoxic doses do no harm but as well no good. Larger doses, however, affected the animals to such an extent that they succumbed to the infection quicker than the untreated controls (Fortescu-Brickdale, Fanoni). The same observation, made by the aforementioned experimenters with streptococcus, was later confirmed by Shaw for pyocyaneous, and by Hill for plague and glanders. Steele recommended the oral administration of formalin (0.5 gm. in a great quantity of water every half hour).

In our efforts to utilize formalin effect, we resorted only

to solutions of urotropin, hexal<sup>4</sup> and neohehexal<sup>5</sup> and also of neosalvarsan. We were led in these experiments by the following theoretical considerations: Since the formalin at the time of its introduction in form of these preparations is not free, it cannot immediately harm the blood cells. Being only gradually liberated in the blood as formalin, its effect might be more lasting. In case of neosalvarsan there might be added the beneficial effect of antibody formation stimulated by the arsenic component. In this latter expectation we felt encouraged by the gratifying results reported for angina by Plaut-Vincenti, for infections of the urinary tract by Singer, Sachs, Gross, Necker, etc. We did, however, not anticipate any striking disinfectant effect from any of these substances. We felt, that if present at all, it would necessarily be restricted and entirely insufficient to combat a streptococcal infection in view of the alkalinity of the blood. This in itself would prevent the liberation of enough formalin to allow a satisfactory concentration in the blood. We administered as a rule intravenously, very rarely subcutaneously, 15 to 20 c.c. of a 15 to 40 per cent solution. In no instance were disagreeable symptoms caused. The effect is well illustrated in a few selected histories.

M. P., thirty-six years old. Admitted June 4, 1918, died June 21, 1918.

*History.*—Last menses Feb. 25 to 28. Since evening of June 1st hemorrhage; on 6th, fetus passed.

*Stat. pres.*—Temp. 38.3 Abortus incompletus mens. III. Blood culture negative.

During next day several chills with temperature rising to 40.2°.

Two intravenous injections of 0.5 gm. neosalvarsan in 10 c.c. of distilled water. Patient stood them well.

Injections fail to influence temperature, but chills seem to come less often.

June 21, 1918. Exitus.

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<sup>4</sup>Sulphosalicylate of hexamethylenetetramin. White crystals soluble in water. Used intravenously in a 10 to 20 per cent solution.

<sup>5</sup>Secondary salt of hexal. Dosage the same.

K. H., twenty-five years old. Admitted Nov. 5, 1917, discharged cured Nov. 17, 1917. (Fig. 3.)

*History.*—On Oct. 30 delivered, placenta removed manually outside of hospital. For past three days fever and chills.

*Stat. pres.*—Temp.  $39.4^{\circ}$ . Purulent discharge. Cervical canal open. Uterine fundus midway between navel and symphysis.

Nov. 6. Intravenously 5 c.c. of 15 per cent solution of neo-hexal. Only 5 c.c. are given instead of 10 c.c. as contemplated because during administration of solution patient became nauseated.

Nov. 17. Without difficulty 10 c.c. of same solution are given. After injection temperature rises to  $40.5^{\circ}$ ; chill.

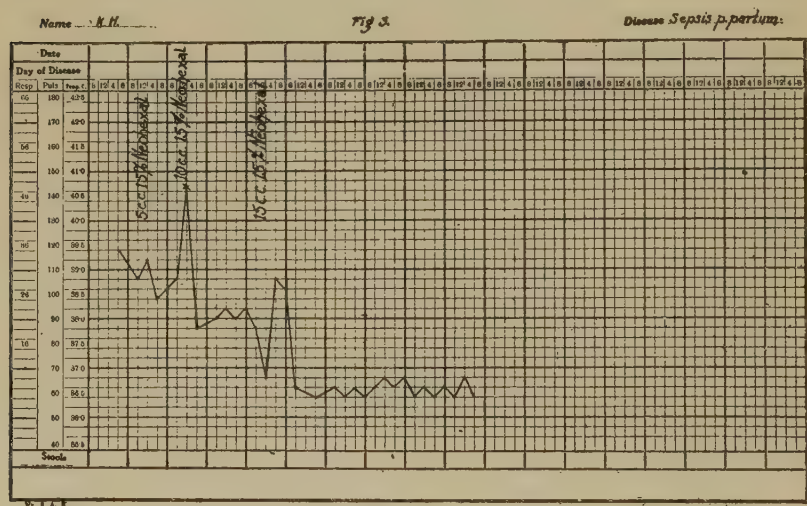


Fig. 3.—Intravenous injection of neo-hexal. Good effect. Patient recovered.

Nov. 19. Temp.  $38.7^{\circ}$ . Another 15 c.c. of the solution given intravenously.

Blood culture still negative.

Next day temperature fell to  $36.2^{\circ}$  and patient remained febrile up to her discharge on Nov. 17.

P. M., forty-one years old. Admitted Oct. 23, 1917, died Nov. 15, 1917.

*History.*—Last menses end of August. On Oct. 15, profuse hemorrhage with passing of tissue. Cured on Oct. 20. Since that day fever and chills.

*Stat. pres.*—Temp. 39.4°. Sanguineous fetid discharge. Uterus retroflexed, easily brought forward, corresponding in size to pregnancy of three months, soft. Adnexa tender, but not enlarged.

Blood culture.—Streptococci, slight hemolysis.

Oct. 29. Since temperature remains high (39.2°), intravenous injection of 10 c.c. of 15 per cent solution of neohepal. No distinct change in temperature curve can be noticed. Therefore injections repeated on Oct. 31, and Nov. 2, 3, 6 and 10. No change in temperature curve.

In subsequent blood cultures distinct reduction in number of colonies. However, this seems only a coincidence, because another blood agar plate made on Nov. 10 is thickly covered with colonies.

With gradual decline, exitus on Nov. 15, 1917.

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H. M., thirty years old. Admitted Nov. 24, 1917, discharged Dec. 22, 1917.

*History.*—Last menses early in May. On Nov. 17, according to statement of patient, entirely spontaneous expulsion of fetus and placenta. Since Nov. 20, fever and one chill.

*Stat. pres.*—Temp. 37.9°. Sanguineous, purulent, slightly ill-smelling discharge. Uterus subinvolved, fundus midway between symphysis and navel. Blood culture sterile.

Nov. 25. Intramuscular injection of 8 c.c. of sterile milk. Three hours later, chill, temp. 39.9°.

On Nov. 26, 29 and Dec. 3, intravenously 10 c.c. of a 20 per cent solution of urotropin. No reaction. Temperature curve absolutely unchanged. Septic remittent type of fever.

Gradually infiltration of left parametrium develops.

On Dec. 22, 1917 patient left hospital against advice.

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Z. A., twenty-four years old. Admitted Jan. 15, 1918, discharged cured Jan. 30, 1918.

*History.*—Last menses three months ago. On Jan. 10, fetus passed. Since that time hemorrhage and fever.

*Stat. pres.*—Temp. normal. Incomplete abortion in third month. Curettage.

Jan. 17. Temperature up to 39.2°. No abnormal palpatory findings in pelvis.

Blood culture: Short chains of streptococci, no hemolysis.

Jan. 20. Intravenous injection of 20 c.c. of a 20 per cent solution of urotropin. No reaction.

On Jan. 21, 22, and 23, 15 c.c. of same solution.



Jan. 24. Gradual fall of temperature to normal. Blood culture negative.

Jan. 30, 1918. Patient well, discharged.

K. A., thirty-seven years old. Admitted Jan. 23, 1918, died Feb. 17, 1918. (Fig. 4.)

*History.*—Last menstruated two months ago. In the morning of day of admission fetus passed. Hemorrhage.

*Stat. pres.*—Retention of placenta, abortion in third month.

Curettage.

Patient, not bleeding, afebrile, discharged Jan. 26.

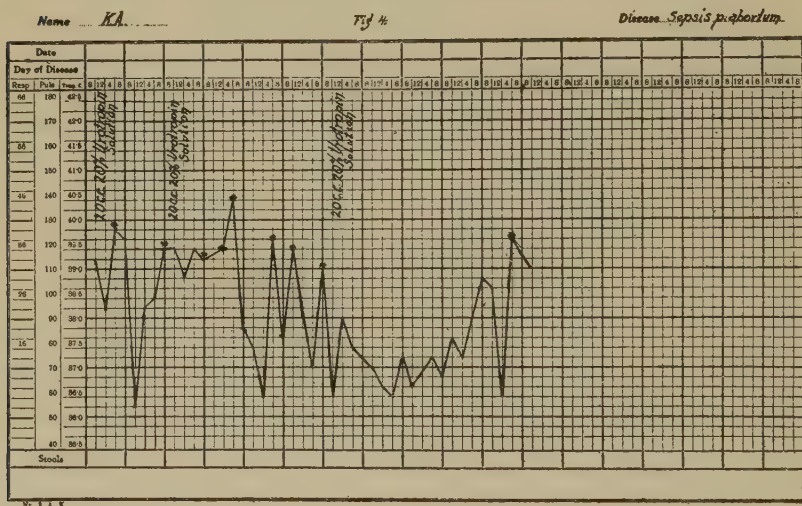


Fig. 4.—Repeated intravenous injections of 20 per cent solution of urotropin, not influencing course of disease.

Jan. 28, 1918. Patient returns to hospital on account of fever and abdominal pain. Uterus well involuted. No anomalies in pelvis. No abnormal findings in heart and lungs. Urine free of albumin, sugar, and gall pigments. Blood culture sterile.

Jan. 29 and Jan. 30, one chill each day.

Jan. 30. Intravenously 20 c.c. of 20 per cent solution of urotropin.

Feb. 1. Injection repeated. Temperature unchanged.

Feb. 5. Had chills daily. Blood culture sterile. Another 20 c.c. of 20 per cent solution of urotropin.

Feb. 8. Had for two days normal temperature.



Feb. 9. Marked general icterus. Patient apathic. Temperature rises, another chill.

Feb. 12. Icterus unchanged. At times delirious, usually somnolent. For past few days gall pigments in urine. Many yellow granular casts.

Feb. 12, 1918. With gradually increasing somnolence, exitus.

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On the whole our results cannot be considered as entirely unsatisfactory. The percentage of recoveries, however, is not large enough to carry conviction of the efficacy of the therapy employed. In our scepticism, the result of critical observation, we feel unable to regard the various preparations of great curative value. It would be an easy task to match every one of these recovered patients with another analogous case that got well under entirely conservative treatment.

**Iodine Preparations.**—Several authors hoped to cure puerperal fever by an inundation of the body with iodine. The methods of introduction of the substance vary. Some of them I have already mentioned: free application of tincture of iodine in the uterine cavity, or packing of uterus with iodoform gauze. Longe passed iodine vapor through the uterus by means of a kinked rubber tube with a hole cut at the kink, so that the return flow of the vapor was secured. This method has been highly praised by Daniel and Costa. Pryor expected not only a local but as well a general systemic effect from the iodoform gauze packed into the pelvic cavity through a vaginal incision. To obtain an iodization of the entire organism he advises to leave the iodoform strips in place for 8 to 10 days, assuming that during all this time the iodine is absorbed from them. In a preceding chapter I have expressed my reasons for doubting that such a general disinfectant effect could ever be obtained in this manner.

Another method consists in the establishing of iodine deposits by means of injection of 10 c.c. of a 25 per cent

solution of iodipin. In intervals of twelve to twenty-four hours three or four more injections are made of 5 c.c. each.

The intravenous administration of iodine more recently has been practiced since Pregl in the solution, which carries his name, found a preparation well borne by the patient. It is a solution which contains free iodine (0.035 to 0.04 per cent) and some of its salts. Unfortunately its exact formula was not revealed and at present a preparation is much employed, idonascin, which on chemical

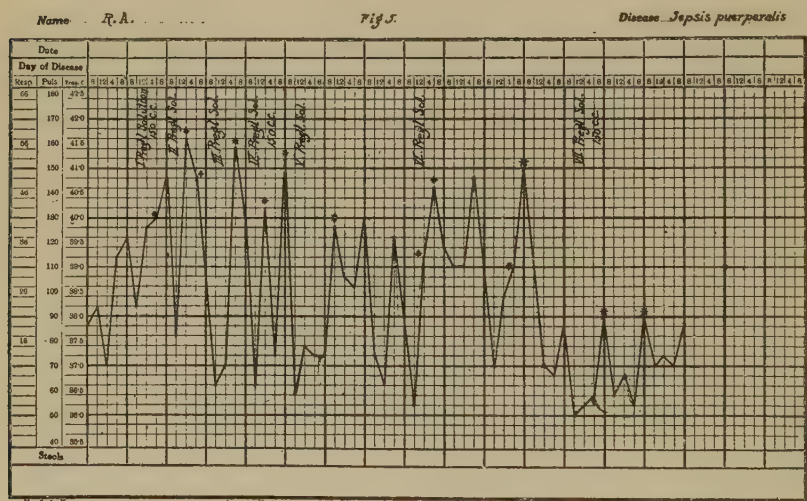


Fig. 5.—Repeated injections of Pregl solution. No effect.

analysis proves identical with the Pregl solution. As predecessor of this method we can regard the intravenous injections of iodine trichloride, recommended in a 1:400 solution by Kocher and Tavel. They yielded no remarkable results.

An intravenous administration of a solution of potassium iodide has been advised by Pick for blastomycoses.

We have experimented with the Pregl solution in a large number of cases, using up to and even over 100 c.c. in several instances.

R. A., twenty-eight years old. Admitted Mar. 14, 1922, died Mar. 30, 1922. (Fig. 5).

*History.*—On Mar. 12, spontaneous delivery with manual removal of placenta outside of hospital. Since Mar. 14 fever and chills.

*Stat. pres.*—Temp.  $37.8^{\circ}$ . Uterine fundus one finger below navel. Cervix admits two fingers. Bloody lochia, no odor.

Mar. 16. Temperature rose to  $40.8^{\circ}$ . Intravenous injection of 150 c.c. of Pregl solution. Blood culture taken.

From Mar. 17 to Mar. 27, fever of remittent type, evening rise to  $40^{\circ}$  and  $41.4^{\circ}$ , morning depressions down to normal. Blood

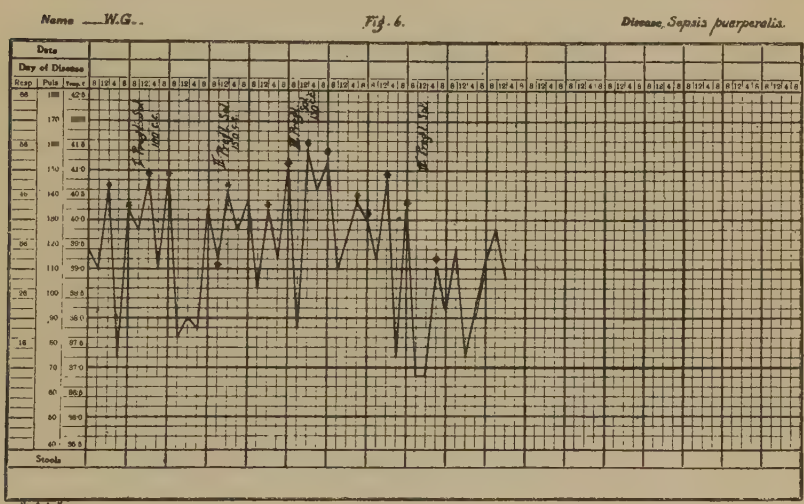


Fig. 6.—Several intravenous injections of large quantities of Pregl solution. Course of disease remains uninfluenced.

culture: Nonhemolytic streptococci. Several injections of Pregl solution, 100 and 150 c.c. (see notations in temperature curve).

Mar. 30. Exitus.

This was a case of severe sepsis in which the Pregl solution failed to show the slightest effect.

W. G., twenty-four years old. Admitted Oct. 22, 1922, died Nov. 6, 1922 (Fig. 6.)

*History.*—Last menstruation on Sept. 2, 1922. Since Oct. 21, vaginal hemorrhage and fever.

*Stat. pres.*—Uterus anteverted, enlarged, soft. Parametria tender.

In view of the condition of the parametria no attempt is made to empty the uterus, but it was hoped that gynergen injections might incite sufficient contractions to cause spontaneous expulsion of retained parts of the ovum.

This effort was successful but also after expulsion of this tissue the temperature continued and patient began to have chills.

Oct. 27. Intravenous injection of 100 c.c. of Pregl solution. No influence on temperature.

Oct. 29, Nov. 1, and Nov. 4, injections repeated, between 100

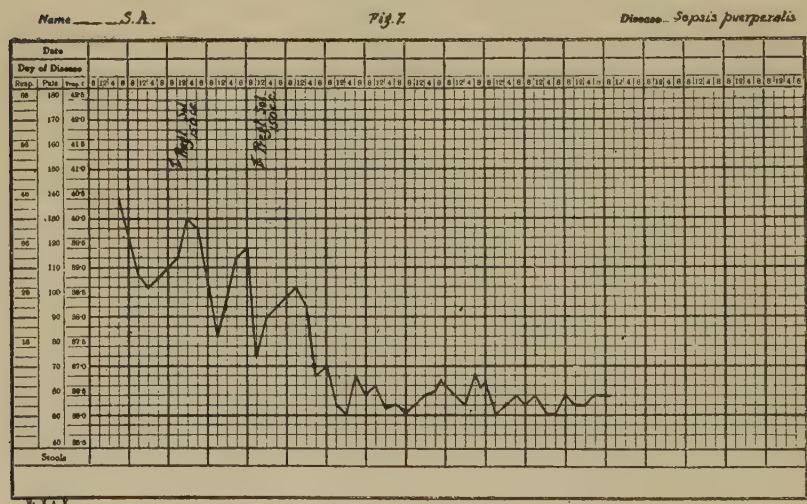


Fig. 7.—Intravenous infusion of Pregl solution. Prompt effect. Recovery.

and 150 c.c. Fever and chills remain unchanged. Patient became somnolent and icteric.

Nov. 6. Patient gradually failed and died.

Immediately on admission patient offered the picture of a severe sepsis. Course of disease conformed to our bad prognosis. All therapeutic efforts failed.

S. A., eighteen years old. Admitted Feb. 26, 1922, discharged cured Mar. 11, 1922. (Fig. 7.)

*History.*—On Feb. 17 spontaneous delivery at term. Since then abdominal pain, fever but no chill.



*Stat. pres.*—Uterus poorly involuted, larger than fist, soft. External os admits finger. Uterine adnexa free. Ergotin.

Feb. 28 and Mar. 2, intravenously, 150 c.c. of Pregl solution.

Mar. 3. Temperature falling.

Mar. 4 until discharge on Mar. 11, 1922, afebrile.

Apparently not a very bad case. The good effect of the infusion became immediately noticeable.

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D. M., thirty-three years old. Admitted May 5, 1922, discharged cured May 18, 1922.

*History.*—Normal delivery fourteen days ago. On fourth day postpartum, fever, on eighth, hemorrhage. For this reason uterus had been digitally explored and a piece of retained placenta removed. Fever ever since with chills up to admission to hospital.

*Stat. pres.*—Temperature 39.6°. Uterus up to navel. Cervical canal open for one finger. Adnexa and parametria free.

May 6. Intravenous infusion of 150 c.c. of Pregl solution.

No influence on temperature or general condition, therefore,

May 8, second infusion of same quantity.

Next day patient afebrile, but on next following day again rise of temperature to 39.8°, therefore,

May 11, third infusion (same amount).

May 12, temperature fell to normal, and stayed normal until day of discharge May 18, 1922.

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L. A., thirty-one years old. Admitted Dec. 24, 1921, discharged cured Jan. 21, 1922.

*History.*—Last menstruation end of November, as claimed by patient, being of usual type. Hemorrhage since Dec. 23, also fever, chills and abdominal pain.

*Stat. pres.*—Temperature 39.3°. Uterus ante-dextroverted. Fundus about 4 fingers above symphysis, distinctly palpable. Along left lateral vaginal wall an elongated thickening, size of penholder.

Dec. 26. Intravenous injection of 150 c.c. of Pregl solution.

Dec. 28. No marked influence on temperature, therefore, same dosis repeated.

Temperature running not so high for next few days while on the left side a periphlebitic mass develops, size of a chicken egg.

This mass afterwards gradually became smaller until only slight infiltrations remained when patient was discharged on Jan. 21, 1922.



Infusion of Pregl solution seemingly had good effect, but more likely the prompt recovery was due to the localization of the process.

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The results of the treatment with Pregl solution on the whole are most gratifying. The percentage of cures amounts to approximately 50 per cent.<sup>6</sup> I shall not attempt to analyze in how far the recovery in each individual case might be due to the injected solution or possibly could be ascribed to certain fortunate circumstances (e. g., localization of the infectious process), but a careful study of the temperature charts here reproduced, together with the appended abstracts of their histories, might justify some doubt that it always was the Pregl solution which effected the final cure.

This is particularly well illustrated in another case which I shall quote:

F. M., twenty-three years old. Admitted May 10, 1922, discharged cured May 26, 1922 (Fig. 8).

*History.*—Last menses middle of December. Since May 9, hemorrhage and fever.

*Stat. pres.*—Slight hemorrhage. Uterus corresponds approximately to pregnancy of four months. External os closed.

Since the right parametrium was somewhat tender it was decided not to empty the uterus instrumentally. Quinine is given to stimulate the uterus to spontaneous expulsion of its contents. At the same time intravenously 150 c.c. of Pregl solution are administered in view of the existing infection. Fetus and large part of placenta are expelled spontaneously, but fever and chills continue. The persistent hemorrhage suggests that possibly a large portion of the placenta is still retained. Excochleation fully proves the justification of this suspicion.

Immediately after curettage temperature sank to normal.

Patient remained afebrile until discharged on May 26, 1922.

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<sup>6</sup>Though the case histories, briefly quoted here, represent only a small part of the cases treated with different preparations, we consider even the total number of our observations too small to allow reliable statistical conclusions concerning the efficacy of the various remedies we have employed in our work.

Only seeming beneficial effect of Pregl solution. Temperature actually becomes normal only after removal of the retained part of the placenta.

Satisfactory results with the Pregl solution should induce one to recommend the Pregl solution; unfortunately, however, it also has certain disadvantages which greatly reduce its actual value.

Right from the start we gained the impression that in

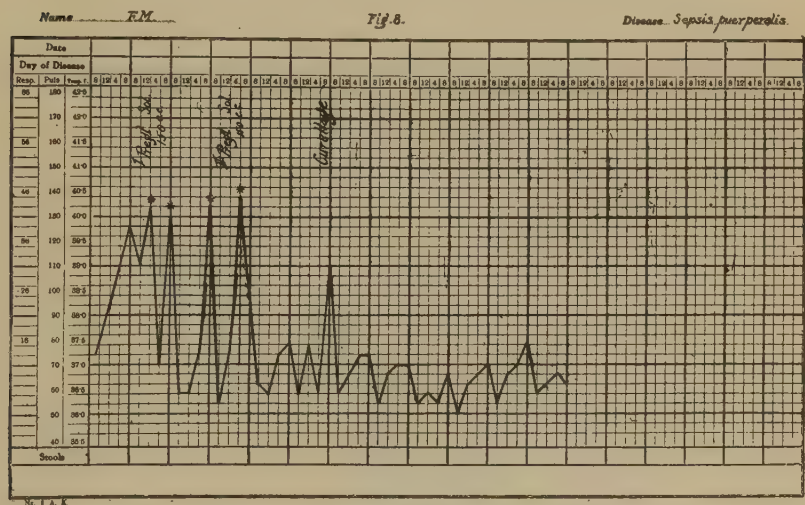


Fig. 8.—Result cannot be ascribed to Pregl solution. Patient becomes afebrile after curettage.

cases treated with the solution, thrombi seemed to form with striking frequency. They usually would extend upward and downward from the site of injection, so that it really became impossible to make many infusions especially into the same extremity. In how far the chemical constitution of the solution is responsible for these thrombi, I am unable to say, but according to the investigations of Mahnert and Santner, Schmerz and others, this process is due neither to a diminution of coagulation time nor to changes in the

intima. Also we failed in the careful study of one case to discover any histologic changes to account for the formation of the thrombus. While the etiology of this most unpleasant consequence remains unknown, its frequent occurrence after the administration of the Pregl solution undeniably is a fact which greatly restricts its usefulness, since every thrombus implies the serious risk of an embolism. Knauer and Hohlbaum actually have recorded one death each, caused by embolism subsequent to an intravenous infusion of Pregl solution. I was also unfortunate enough to see a young woman die immediately after the administration of 150 c.c. of this solution.

This patient was twenty-four years old. A few days after a spontaneous delivery she had a temperature rising to 40°. The first injection of 100 c.c. was borne without discomfort. Also after the second injection on the next day patient seemed to be undisturbed. But only a half hour later she had convulsive contractions of the extremities. She became delirious, later unconscious and died within an hour.

The clinical picture did not correspond to that usually seen in a case of embolism, and I assume that in this instance an unusual permeability of the vessel walls, led to a sudden inundation of the body with iodine so that the patient died of an acute iodine intoxication.

This one observation suggests that it probably is wiser to refrain in seriously sick patients from the intravenous injection of any drug that acts as drastically as the Pregl solution or e. g., tryptaflavin.

Another iodine preparation, mirion,<sup>7</sup> we tried in a few cases either alone or in combination with other drugs, but failed to notice curative effect even in a single instance.

M. H., twenty-eight years old. Admitted Feb. 28, 1922, died May 2, 1922. (Fig. 9.)

*History.*—On Feb. 12, at term, delivered of twins. First child born spontaneously. Second lying in transverse position turned

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<sup>7</sup>An organic iodine solution containing 1.7 per cent of free iodine.

and extracted (outside of hospital). Since then fever and chills. Patient at times somnolent.

*Stat. pres.*—Uterus size of small fist, soft. External os closed. Hard infiltration of left parametrium.

In the beginning, temperature rises only moderately, no chills. Heart action unsatisfactory, constant arrhythmia. Since the case seemingly is fairly mild and the process apparently was localized in the parametrium, at first only conservative treatment is resorted to; digitalis, in view of cardiac disturbance.

When later chills appeared (see appended temperature curve) five injections of mirion were given (usual dosage is from 5 to

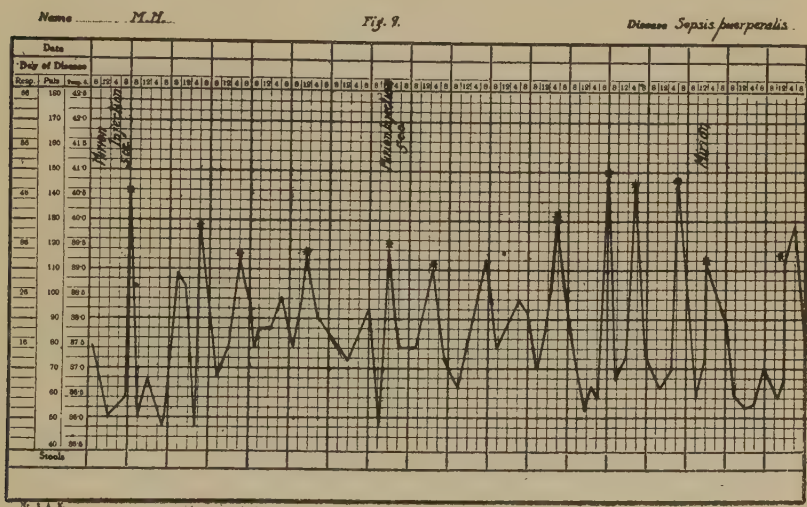


Fig. 9.—Several injections of mirion. No effect.

20 c.c. subcutaneously or intramuscularly). No apparent influence on course of disease.

Patient died on May 2, 1922.

This at first looked like a favorable case with localization of the infection. It seems unlikely that the course would have been different if mirion would have been injected earlier, since autopsy revealed extensive thrombosis reaching into the iliacae communes. Neither their origin nor further development could have been influenced even by earlier medication.



In the group of the iodine preparations belongs yatren<sup>8</sup>, containing 25 per cent of iodine. Originally under the name of tryen recommended by Abel in the treatment of specific and nonspecific vaginal discharges, this preparation, on account of its nontoxicity, soon as well was employed as a systemic disinfectant. Experimental investigations made by Becker, however, showed that even in concentrations unobtainable in the body fluids it does not inhibit bacterial growth. Therefore, any beneficial effect that is ascribed to this substance could be explained only as due to foreign substance stimulation. Some authors emphasize that it never causes local reactions, while others complain about the infiltrations resulting from the injections. The usual dosis is 2 to 4 c.c. of a 5 per cent solution. It has been given also in larger doses, but the latter may cause a nephritis. Zieler and Birnbaum reported two cases of acute yellow atrophy of the liver in patients treated with yatren. They recommend to exclude all patients with hepatic lesions from this therapy and advise great care in every case. Urine must be examined daily for urobilin, urobilinogen, leucin and tyrosin so that even the slightest disturbance of liver function would be recognized promptly.

We have never tried yatren and thus have no personal experience with it. I shall later speak of yatren-casein.

**Chloramine T.**—Copeland believes to have found a really valuable remedy in clorazena (chloramine T). He dissolves 13.8 grains of this substance in 100 c.c. of cold, sterile water and then adds 400 c.c. of sterile physiologic salt solution. This represents the maximal dosis for one intravenous injection, which might be repeated four or five days later. He claims to have cured 10 out of 12 patients treated

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<sup>8</sup>Iodoxychinolinsulphonic acid, to which is added 20 per cent of sodium bicarbonicum. A yellow powder soluble in hot water. Often used in combination with caseosan for nonspecific stimulation.



in this manner. I do not think that this method is known in Europe or ever has been tried here.

**Animal Coal.**—In a preceding chapter I took occasion to refer to some experiments I have made with an animal coal. I attempted to bind the endotoxins produced by streptococci to a coal emulsion and thus to render the bacteria at least partially innocuous. After having tried the emulsion in cases of peritonitis, without noteworthy effect as pointed out, we thought to test its applicability to the general systemic infection and injected intravenously an emulsion, specially prepared for me by Merck (incarbon).

We began with very small doses, 10 to 20 c.c., which were well borne, so that with gradual increase we finally reached a dosage of 100 c.c. One final observation induced us to desist from any further trials.

A patient had received, without any untoward effects, two incarbon infusions of 60 and 90 c.c., respectively, when she unexpectedly died during a third infusion. In spite of the purity and uniform consistency of the emulsion we naturally thought first of an embolism through larger carbon particles. A carefully done necropsy revealed no trace of an embolus and the coroner ascribed death to collapse, such as might occur during any, even slight, operation.

Though the postmortem findings actually proved the apparent harmlessness of this therapy we did not care to use the emulsion any longer particularly because we had no evidence of any beneficial effect. As a matter of fact all our cases with a general infection up to that time had died, but the few cases of peritonitis we saw recover while using the emulsion might have recovered also without this medication.

Further pathologic-anatomic and histologic investigations convinced us that the intravenous administration of this carbon emulsion really does not justify any hope that it could possess any curative value. Reverting once more

to its employment in cases of peritonitis, when we poured one or two liters into the abdomen, I shall mention the interesting fact that some of the coal particles evidently had entered and clogged up some of the lymph vessels which could be seen at autopsy as black threads leading to black lymph glands. In postmortem examinations of patients who had died some time after the operation the entire peritoneum showed a slate-gray discoloration, while the lymph vessels again were found free of the absorbed coal particles. These pathologic-anatomic observations prove that the coal particles actually block some of the lymph channels and that the therapy might be of some limited value in cases of peritonitis, not too acute and foudroyant, by impeding resorption. The coal emulsion certainly cannot interfere with resorption that takes place from areas where the endothelial covering is destroyed, which is the case in every fully developed general peritonitis when circulation is seriously impaired.

This merely mechanical effect obviously cannot come into play with an intravenous injection of the emulsion in cases of systemic infection. Whenever we had the opportunity we searched meticulously all the organs, macroscopically and microscopically, for such coal particles, and only with great difficulty could we discover here and there a trace of them in a vessel lumen or perivascularly located (lungs, kidney, spleen and bone marrow). It is impossible to speak of an actual imbibition of either tissues or lymph vessels. Occasionally a few particles were found in a centrifuge sediment of urine. Even a dosage of a total of 300 c.c., given as the maximum in any one case, would be entirely insufficient to inundate all the tissues for an effective binding of all toxin. We calculate that for this purpose at least 500 to 1000 c.c. or even more would be required as a single dose. It remains an open question whether such quantities could be introduced without danger or whether

this might not cause a carbonoxide intoxication from certain almost unavoidable impurities of the emulsion (Izar).

However, it is unlikely that even these large doses would fulfill their purpose, because as in the intravenous administration of colloid metals, we would have to reckon with the rapid disappearance of the coal particles from the circulating blood and their prompt deposition in liver, spleen and bone marrow. Of course, they would there still maintain a certain relation to the blood but not that intimate contact with the total amount of blood which is essential for making them capable of coping with large quantities of toxins by quick adsorption.

### Colloid Metals

**Silver Preparations.**—A notable divergence of views prevails concerning the value of such colloid metals as col-largol, electrargol, dispargen, argosan, and others of the same type in the treatment of puerperal fever. They have been extensively tested for some time now.

Originally it was thought that it must be possible with them either to destroy or at least to reduce the virulency of pathogenic bacteria. Many experiments on animals and observations at the bedside, however, have greatly weakened any such belief. Many investigators, and I myself, are at present convinced that any good effect of these remedies at least in part is due to the resulting hyperleucocytosis, in part also to their general stimulating effect.

When Naegeli first reported his well-known experiments which demonstrated the deleterious influence of metal colloids on spirogyres, the idea naturally suggested itself that a similar destructive or at least growth-inhibiting action might be expected as well in relation to bacteria in the blood stream. This idea seemed further justified by the fact that this very effect had been observed by addition of such metals to infected solid and liquid culture media.

It seems useless to enter here into the details of this problem, since the papers of Saxl, Pfeiffer and Kadletz, Baumgarten and Luger, and of myself, have dealt thoroughly with them, and especially because more recent contributions, in my opinion, have made this already complicated problem rather more obscure than clearer. The simpler interpretation of the oligodynamic action of these substances on the basis of their colloid nature has been replaced by a theory of surface phenomena.

I have made some experiments along this line hoping that their results might be applicable to the therapy of puerperal infection, and for this reason I shall say a few words about them, particularly because I think that these investigations clearly support those authors who consider mysterious and complex explanations of the action of the metal colloids as entirely superfluous. (My views are given in detail in the paper published in the *Zentralblatt fuer Physiologie*, 1919.)

When a piece of zinc wire is placed on an agar plate, a white halo develops around it, a few millimeters wide. The agar, now dissolved, shows a zinc reaction, and further investigations demonstrated that the zinc contents of the agar diminish proportionately to the distance from the original location of the zinc wire. Around the whitish area was found another ring, again several millimeters wide, which was sterile, while farther off, all around the white halo, bacterial growth was even. The sterile area surrounded symmetrically the white area, its shape being determined by the shape of the piece of zinc placed on the agar plate. Similar observations were made with other metals, e.g., copper.

Analogous but not as evident were the results of experiments in which the effect on plant growth was determined. Equally densely seeded plant pots were watered either with pure water or with water that had been kept for some time



in vessels containing pieces of copper, zinc or silver. As a rule those of the second group showed that not all seeds had developed and that the growth of the plants was retarded. No conclusions, however, could be drawn because in some of the pots of this second group growth seemingly was more luxuriant than in some of those wetted with pure water.

The more plausible explanation, that we are dealing solely with the effect of a metallic salt solution and not with most complex phenomena, is also accepted by Spiro. He was able to demonstrate the presence of copper ions in distilled water which for some time had covered a piece of copper. Also Gottschalk and H. H. Meyer ascribe the oligodynamic effect solely to a solution of metals. As proof for this contention, must be accepted the experiments of Pfeiffer and Kadletz. They first had concurred in the views of Saxl, but later observed that the decolorization of a solution of fuchsin produced by copper in substance is identical with that obtained by the addition of a copper colloid solution diluted to 10-12. This same identity of effect of either copper in substance or a copper colloid solution was likewise established by Baumgarten and Luger for ferments.

Since I myself observed in experiments retardation of growth for bacteria but occasional stimulation for plants, extreme care in the therapeutic application of such metal solutions seems essential. Such solutions, if found therapeutically useful, would offer over colloids the great advantage of cheapness and of ready availability, since they could be easily prepared anywhere. There is no intention on my part, however, to claim that these laboratory results prove anything concerning the therapeutic value of metal solutions, or that they show any parallelism of effect between metal and colloid solutions. It must be remembered that colloid metals are of a different chemical structure.

Both types of solutions have only the one fact in common that they represent an extremely fine distribution and thus an enormous increase of surface. Obviously I am unable to state how many times larger the colloid particle is than the metal particle but I feel certain that the difference in size is great, since we cannot see under the microscope with the greatest available magnification metal particles, while the ultramicroscope shows the colloid particles clearly as shining discs on the black background.

These differences might be of importance from the viewpoint of therapeutic effect because the efficacy of the colloid metals is dependent upon the degree of dispersion. Rather generally the higher efficacy of colloids prepared by electric process as compared with those chemically produced is explained by the smaller size of the particles of the former group. My own investigations do not support this contention and, therefore, I do not think that theoretically a greater oligodynamic effect could be expected from the metallic salt solutions. In two cases of surgical sepsis, which in general offer a better prognosis than cases of puerperal sepsis, I have employed a saline solution, which for considerable time had been kept in contact with silver. In neither case any definite good effect could be ascertained.

Returning again to the theme under discussion, I consider it unnecessary to describe the chemical characteristics of colloids or the modes of their preparation, since the reader can find all the desired information in textbooks of physiologic chemistry.

There are quite a number of colloidal silver preparations on the market. The oldest of the group is collargol (Heyden) introduced into therapy by Credé in 1895. This preparation contains 75 per cent silver and 25 per cent albumin, the latter required to keep the metal in form of a colloid. Its effect according to Credé is bactericidal, and at first he absolutely denied any resulting hyperleucocy-

tosis. Later he had to yield on this point. For some time writers spoke of a catalytic, ferment-like activity of collargol, an oxidation process started even by minute quantities of the substance. This theory proved useful for explaining the claimed good results of such small doses as, e.g., 10 c.c. of a 2 per cent solution, certainly a minimal dose when distributed through the total blood volume. Only very few authors admitted such a catalytic function and then only with certain restrictions (Bamberger, Netter and Salomon, Albrecht). Most of the experimenters arrived at quite different conclusions.

Hoffmann, in rabbits, observed a marked leucocytosis, and other investigators, Brunner, Majewsky, Rodsewicz, Acan and Weil, Dungern, etc., confirmed this observation. This change in the blood picture is not lasting. There is first a hypoleucocytosis, and only a few hours later the hyperleucocytosis becomes manifest with an increase in the polynuclears and a diminution of the lymphocytes. After about twenty-four hours the original blood picture is restored. This return occurs quicker after intravenous administration, slower after subcutaneous injection or percutaneous application in form of a salve, so that in every case repeated administration is required. Weichard, as early as 1907, had discovered that repeated injections of nontoxic chemicals (colloid metals) will produce in animals a state of fatigue, followed after rest by an increase of energy. This is a phenomenon not unlike that seen after the injection of albumin derivatives, being actually due to their formation. According to R. Mueller albumin-like colloids exactly like albumoses cause signs of anaphylaxis, very similar symptoms being produced as well by colloids free of albumin. I shall return to this point in the next chapter when speaking of vaccines.

If collargol yields any effect it, therefore, in the main

is due to the production of a hyperleucocytosis though even this result is not constant.

Dael, in 1913, showed that, e. g., electrargol, given prophylactically or shortly after infection, (intraperitoneal infection with virulent germs) not only fails to show any curative power but indeed proves harmful, and exhibits any effect at all only if the bacteria are of low virulence. *In vitro* this substance is bactericidal, as also proved by Probansky and Seibert, but solely in a concentration of 20 per cent. Such strong solutions, however, cannot be employed in the animal experiment and certainly not on a patient where one must limit himself to 2 per cent and a maximum of 5 per cent solutions. If the injected solution has a concentration so far below that required for bactericidal effect, its dilution in the blood necessarily will reduce its antiseptic efficacy to practically nothing. Calculated to the total blood volume, the injected collargol would represent a concentration in the blood of approximately 1:10,000 and therefore any interpretation of seeming good effect of collargol on the ground of its bactericidal power (Credé, Bondy) must be repudiated. For some time Cohn, Tromsdorf and Brunner had denied, as the result of their experiments on animals, that the soluble silver salts had any therapeutic value.

Some investigators grant them a limited antitoxic effect, but according to Hoffmann the opsonic index is raised neither in the animal nor the human being by the administration of colloid metals.

Experiments, we then see, never established a specific and especially a bactericidal action for metal salts. It must be added, that most of these experiments were undertaken in the assumption that the introduced hydrosols would circulate in the blood for some time so that they would exert a more continuous effect. That this, however, is not the case has been shown by the investigations of Voigt which fur-



nished reliable information concerning the fate of intravenously introduced metal colloids. All this convincingly explains their weak disinfectant and correspondingly slight curative effect.

In most painstaking studies Voigt found that silver particles after a very short time can no longer be discovered in the blood, that only faint traces of them appear in urine or feces. They had become promptly deposited in liver, spleen, kidneys and bone marrow. This elimination from circulation in so short a time necessarily greatly curtails their possible beneficial activity in the blood on which we base all our faith. However, the circulating blood still maintains some contact with the metal deposits in these various organs, and therefore, there actually remain two possibilities of their further action: (1) a catalytic function, though greatly reduced; (2) some of the metal might be dissolved, and thus returned into circulation in small but constant quantities to continue its effect.

These small fractions of the originally given dosis are not apt to prove of great therapeutic value, since, as I have pointed out, not even the total dosis in its dilution in the blood would suffice to destroy the bacterial contents of the blood. It certainly would be inconceivable that these minute amounts could affect the bacteria in the main focus of infection or in secondary foci as, e. g., in thrombi, which are practically eliminated from direct contact with the blood stream.

Much less, if anything at all, could be expected from the intramuscular or subcutaneous application of these substances. They are deposited at the site of injection and thus *a priori* deprived of any chance of yielding a beneficial effect within the blood which in fact they probably never reach.

My own careful clinical observations could never convince me that they exert either an antibacterial or an anti-

toxic effect. Innumerable bacteriologic blood studies showed in not one case, even after repeated injections of collargol, the slightest reduction of bacterial contents. Animal experiments and theoretical considerations really never justified any expectation that it could be otherwise. Antibacterial, without simultaneous antitoxic, effect as a matter of fact would be directly harmful. Considerable destruction of bacteria would inundate the body with an amount of toxins which would prove disastrous if there were no agent at work at the same time to counteract this profound intoxication. Again, antitoxic without bactericidal effect would be of no benefit, especially in the case of the streptococcic infection.

Deprived of any hope to destroy bacteria with collargol, we are forced to put our faith solely on its leucotactic action and its possible general invigorating effect. Most observers agree that a marked hyperleucocytosis follows the injection, and my own observations in many puerperal infections treated with collargol almost invariably showed a primary hypoleucocytosis followed by a rapid increase in the number of leucocytes with subsequent reduction and gradual return to the original count within approximately 24 hours. Studies recently renewed both on puerperal fever patients and, during the war, in septic soldiers led to identical results.

As before, we again made the definite observation that a lacking reactive hyperleucocytosis usually means a slim chance for recovery, an observation which seems of an equally unfavorable prognostic significance practically for every form of therapy of puerperal infection.

Bamberger thought that a large number of leucocytes is required for the prompt removal of the silver from the blood and that thus the hematopoietic organs are forced to furnish a reserve supply, which fact accounts for the primary hypoleucocytosis and the secondary hyperleucocy-

tosis. This theory has not been proved but seems reasonable.

Outside of collargol we have made use of electrargol, dis-pargen, fulmargin, argosen and similar preparations, also of colloids of other metals, e. g., nickel, copper and gold. The immediate effect of all of them is about the same. As a rule we administered them intravenously, only rarely subcutaneously and intramuscularly, never as an enema. We have no personal experience with collargol in the form of salve or with its administration by mouth. Most commonly we infused between 5 and 10 up to 20 c.c. of a 2 per cent solution. For the preparations marketed in the form of sealed ampules, special sterilization is not required. These when old often show a silver mirror on the glass wall which does not indicate deterioration of the product. If, however, large particles of precipitation are noticeable, the ampule should not be used for intravenous and preferably not even for intramuscular injections. This precipitation denotes changes in concentration, which render the solution unreliable for use. For such injections it is unnecessary to expose the vein or to produce a local anesthesia.

If the infusion is made slowly, the patient usually experiences no discomfort. Very rarely she would complain of a feeling of oppression, dyspnea or scintillations, symptoms which disappear quickly. Care must be taken lest some of the colloid be injected into the tissue around the vein. Painful infarcts might be the result, not rarely leading to necrosis and abscesses. These untoward sequelae are never seen after intramuscular or deep subcutaneous injections which prove more painful to the patient and, as pointed out, probably are still less effective than intravenous infusions.

Often, but not always, the latter are followed by a chilly sensation, at times with actual rise in temperature, which might be looked upon as a favorable reaction. Its cause is

not known. Some ascribe it to a destruction of leucocytes, others to that of bacteria, while Dungern regards it as due to an intoxication with ferments.

Personally I feel that this reactive chill is analogous to the chill observed after intravenous injection of vaccine or serum, representing a violent reaction to the parenteral introduction of a foreign protein which actually is present in these solutions. Such an explanation seems acceptable and makes other complicated interpretations of the phenomenon quite superfluous.

In a very small percentage of instances the injection causes a critical drop of the temperature, in a few others the fall is slow, extending over a day or two, but in the majority of the serious cases the temperature actually remains uninfluenced.

In the cases with a sudden drop of temperature the effect resembles closely that of vaccines or other albuminoid substances, though one can hardly think of any specificity in the action of these metal preparations. In the cases with a lytic fall of temperature a beneficial effect of the injected colloid is strongly suggested because the hyperleucocytosis and a catalytic action resulting from the primary contact of the metal with the bacteria in the blood might conceivably have reduced their virulence and thus caused the temperature to become lower. How very inefficient, however, such an assumed effect is in the therapy of puerperal fever is amply shown in the regrettable fact that very often the temperature again quickly rises.

Any specific action—in which I, myself, do not believe—moreover could affect only those bacteria or toxins which are in the circulating blood. The tendency toward formation of thrombi, characteristic of puerperal infections, not only causes the largest part of the truly infectious material to be safely protected against the colloid in the blood, but also helps to establish many new foci from which bacteria



and toxins continue to invade the body. This likewise holds true for the usual primary port of infection, the uterine cavity. The relatively poorly vascularized endometrium is almost, and the infected and necrotic tissues completely cut off from the blood stream which transports the healing remedy. This is the very reason that in the thrombotic type of puerperal fever one or a few injections can yield absolutely no results, and repeated injections could be of benefit solely if, perchance, they are made just at the time when a fresh bacterial or toxic invasion takes place. Therefore even this problematic good effect will hardly be achieved when injections are given schematically in intervals of 12 or 24 hours. As long as we regard the chill as a sign of a new invasion, more faith might be placed in a routine of making the infusion always very soon after a chill.

For these same reasons we cannot expect too much even from the resulting hyperleucocytosis. The bacteria within the thrombi obviously are not any more accessible to the leucocytes than we have shown them to be to the metal colloids in the blood.

Therefore, great skepticism must be felt concerning any possible curative value of any of these preparations including those manufactured by an electrolytic process in spite of their finer dispersion. If we luckily observe improvement it is not necessarily to be credited to the employed remedy; we see it occur too often even without any therapy. But since in general these preparations are harmless, if properly administered, and since they might be effective, e.g., in the lymphogenic type of infection, there can be no objection against their use in conjunction with other therapeutic measures. It probably makes no difference which one of the various colloid metals is applied.

Their use, however, is not entirely free of occasionally very disagreeable by-effects. I can illustrate this by a re-

cent experience with "concentrated collargol" (Heyden), a preparation which before administration must be rendered isotonic with a substance furnished in another ampule.

In a primipara, thirty-one years old, after seventy-two hours of labor (due to rigid cervix, primary atony and premature rupture of membranes) it became necessary to make cervical incisions and apply a high forceps. After a light rise of temperature during the first few days postpartum, on the eighth day the patient had a chill with a temperature of 39.8° C. We injected "concentrated collargol" intravenously. The immediate effect was so frightful that for a few hours we expected the patient to expire.

A few minutes after the infusion the patient had an intense chill. She was cyanotic, dyspneic, pulse irregular, at times the heart actually stopped beating. We repeated several large doses of camphor and caffeine. Under continued stimulation chiefly with strychnine patient slowly recuperated slightly. About half an hour later another serious collapse followed. Patient was pulseless, her skin had a dark blue hue, she became somnolent and then had a severe hemoptysis. Coughing a few times she expectorated a large amount of red foamy blood. Again stimulants were applied. Approximately eleven hours after the collargol injection—the hemoptysis in the meantime had stopped—a severe uterine hemorrhage began which required immediate packing of the uterus and could be completely controlled only within twenty-four hours with further administration of ergot and pituitrin. Finally patient recovered.

It is difficult to explain such alarming consequences. In part in this case they were due to a constitutional inferiority of the patient. She was of a typical angioneurotic habitus and exhibited a marked dyscrasia also against many other drugs. She suffered early in pregnancy from exaggerated vomiting which the attending physician had tried to control with adrenalin. The injection of a very small amount of a 1:10,000 solution caused most disagreeable symptoms, at times actual collapse. When during labor quinine and later a little pituitrin was given, the patient showed marked sensitiveness to both, and when I tried postpartum to control the hemorrhage, with pituitrin, she collapsed. Though

the severe reaction in this patient partly is to be blamed on her constitutional peculiarities, the injected collargol certainly as well must have greatly contributed to the alarming condition. One might think of a pulmonary embolism, although a lung infarct as a rule will not become hemorrhagic in so short a time, or of some sort of violent anaphylactic reaction. This is unlikely to occur after but one injection, but it is possible that in a hypersensitive patient, as our patient undeniably was, the preceding injections of other organ extracts may have led to sufficient sensitization to release a severe anaphylactic reaction with the administration of collargol. It is also possible that a technical error was made in the required isotonization of this preparation before infusion. I certainly would feel loath ever to use it again, especially because other preparations of this sort probably imply much less risk.

Also in literature we note reports of untoward sequelae of collargol injections. Klauhammer recorded general aggravation of the condition of the patient, Makelaire reported an hysterical attack, Caubet, Baum, and Courant several observations of thrombosis and pulmonary embolism and necrosis of the fascia. Latzko described a case of uremia, Haak one of anuria as the result of thrombosis of the renal vein. Bonnaire saw severe hemorrhages from the gums, Cohn from the uterus, requiring packing. The latter thought that the hyperleucocytosis reduces the coagulability of the blood. Bondy reported a death, and Cyffer repudiated collargol therapy as too risky.

Petitjean demonstrated on animals that 0.05 to 0.1 gm. of collargol per kg. weight in intravenous injection will cause a quickly fatal edema of the lungs, moreover marked congestion in all parenchymatous organs and especially in the gut.

Not more encouraging are the reports concerning iodecollargol.

A few words must be said in regard to the combined application of two or more of the colloid metals.

We have employed such combinations occasionally, not in the idea of obtaining some particular compound effect, but only incidentally when the first or second preparation administered did not seem to do any good. No visible benefit was derived from any of these combinations. However, there exist reports in literature of cases in which two colloids had been deliberately injected simultaneously with seeming advantage to the patient. These attempts are based on certain experiments of Bechhold which tend to show that the mixture of two metal colloids in the test tube exhibits a higher antiseptic power than each singly. He explained these findings by means of "dispersed galvanic chains" developing in the contact of two metals, e.g., copper and silver, or silver and platinum. They cause the less precious of the two metals to be dissolved, the solution being endowed with a marked bactericidal energy. In the living organism, he assumes, the beneficial effect is due to the fact that the very organs, in which the colloids are apt to be deposited (liver, spleen, kidneys, bone marrow), are as well the favorite sites for the accumulation of bacteria which thus come more directly into the sphere of the destructive influence of these galvanic chains.

Gratifying clinical results with metal combinations have been recorded by Eufinger, who employed platinum-silver and gold-silver (Heyden), and by Herschan with silver-copper (cuprocollargol, Heyden). According to the theory of Bechhold the good effect in the first two preparations would have to be ascribed to the silver contents, in the last mentioned colloid to the copper contents.

The number of these reports is too small to justify positive conclusions concerning the value of these combinations. Our very limited experience with them has not altered our diffidence. Dispersed galvanic chains could not form in the



thrombi, the well protected shelters of bacteria, or in the circulating blood, which carries the germs from place to place. Thus these supposedly important galvanic chains would be deprived of the possibility to display their sanative activity just in the places where it is needed the most. The chief argument of the advocates of colloid mixtures is, that the highest galvanic effect will occur in those organs in which the bacteria are most apt to be deposited. Our investigations reveal that in these parenchymatous organs only a few and very small metal deposits can be discovered. These will develop only a minute amount of electric energy and therefore contribute but little to the destruction of bacteria within these organs. On the whole we consider this problem also as still another example of the impossibility of simply transferring the results of laboratory tests into practice.

Finally the fact might be mentioned that metals, also in noncolloidal form, have been employed in the treatment of puerperal infections. Thus Noire recommended ammoniacal copper sulphate (about 4 per cent), given daily, morning and evening in doses of 2 c.c. until the temperature has become normal, which is supposed to occur after three days. We have never tried it.

I shall briefly quote a few illustrative histories of cases in which we administered metal colloids.

F. J., twenty-four years old. Admitted Mar. 14, 1918, died Mar. 22, 1918.

*History.*—Last menses early in January. Patient claims to have aborted spontaneously on Mar. 10. Since that time high fever with chills.

*Stat. pres.*—Temperature  $39.2^{\circ}$  C. Bloody discharge. Uterus anteverted, enlarged, soft. Cervical canal open. Adnexa free.

Mar. 16. Condition unchanged. Icteric discoloration of sclerae. Blood culture: Pure culture of streptococci.

Mar. 17. Icterus more marked. Severe pain in joints. Intravenous injection of 0.2 gm. collargol. After injection temperature rose to  $40.5^{\circ}$  C. without chill.

Mar. 18. Condition and temperature unchanged. Another injection of 0.2 gm. of collargol. No reaction.

Mar. 19, 20, and 21. Daily injection of 0.3 gm. of collargol. No influence on course of infection noted. No marked increase of leucocytes, rising from 5000 before injection only to 6500 after it.

Mar. 21. Icterus greatly increased. Both knee joints swollen. On both lower extremities large red blotches.

Mar. 22, 1918. Exitus.

In spite of several injections of collargol the serious infection was not influenced in the slightest degree. In view of the slight leucocytic reaction our prognosis was unfavorable and the outcome not surprising.

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K. M., thirty-five years old. Admitted Oct. 22, 1918, discharged cured Nov. 16, 1918.

*History.*—Last menstruation end of July. Hemorrhage since Oct. 14. Next day fetus passed.

*Stat. pres.*—Purulent fluor. Uterus retroposed, small. Right parametrium slightly tender to pressure. Endometritis post abortum.

Oct. 18. During preceding few days temperature up to  $40.5^{\circ}$  with three chills. Therefore milk injection. Injection followed by rise of temperature but no chill.

Oct. 29, 30, and 31, daily intravenous injection of 10 c.c. of 2 per cent solution of collargol, well borne.

Beginning Nov. 1, temperature remains below  $37.0^{\circ}$ . Extensive infiltration develops in right parametrium.

Nov. 16, 1918. Patient discharged cured. All blood cultures sterile.

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K. R., twenty-four years old. Admitted June 25, 1918, discharged cured July 8, 1918.

*History.*—Two days ago premature birth in seventh month. Patient claims to have had a chill immediately afterwards and several more before admission.

*Stat. pres.*—Uterus not firmly contracted, no other abnormal findings.

Blood culture sterile.

June 26 and 28. Intravenous injections of 10 c.c. of dispartgen (2 per cent).

June 29. Same solution, 15 c.c. intravenously.

All injections well borne, only once followed by chill.

July 1. Temperature began to fall.

Patient remained afebrile until discharged well on July 8, 1918.

K. G., thirty-one years old. Admitted July 29, 1916, died Aug. 10, 1916. (Fig. 10.)

*History.*—Last menses Apr. 23. For past eight days uterine hemorrhage, passing of pieces of tissue. Fever and several chills.

*Stat. pres.*—Temperature 38.0° C. Incomplete abortion, third month. By means of curettage ill-smelling pieces of placenta are removed.

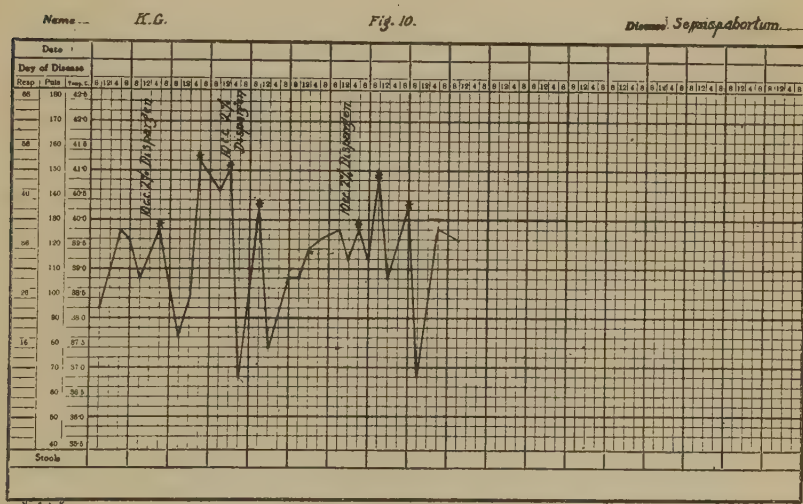


Fig. 10.—Repeated intravenous injections of dispartgen. No effect. Infection takes its course uninfluenced.

During next days high fever with many chills.

Blood culture: Streptococci, markedly hemolytic.

Aug. 2, 4, and 7. Three intravenous injections of 10 c.c. of 2 per cent solution of dispartgen. No influence on temperature or general condition. Several chills.

A few days before death a lobar pneumonia on left side developed leading to exitus on Aug. 10, 1916.

A. P., twenty-six years old. Admitted June 29, 1918, discharged cured July 12, 1918. (Fig. 11.)

*History.*—Patient delivered spontaneously in hospital. Dura-

tion of labor was three hours. Temperature at time of admission 38.6° C.

For the first few days of puerperium daily rise of temperature to 39.6° C.

July 3, and 5, intravenous injections of 10 c.c. of 2 per cent solution of disargen. Temperature rising after injections with severe chill.

A day after last injection temperature sank to normal and remained normal up to discharge on July 12, 1918.

Blood culture sterile.

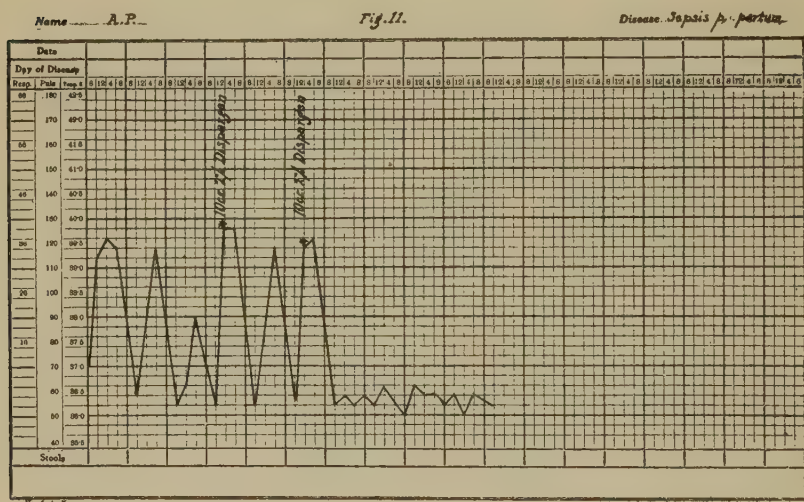


Fig. 11.—Two injections of disargen with good effect.

W. L., thirty-two years old. Admitted July 17, 1918, died Aug. 3, 1918.

*History.*—Last menses end of May. Since July 12 fever and chills.

On July 14, fetus had passed. Placenta was removed with curette. Fever continued up to admission.

*Stat. pres.*—Brownish fetid discharge. Uterus somewhat enlarged, soft. At the base of the right parametrium a thin (size of little finger), round infiltration palpable. Metrophlebitis.

Blood culture: Pure culture of hemolytic streptococci.

July 18, 19, 20, and 21, daily 10 c.c. of 2 per cent disargen intravenously.

No influence on temperature or general condition noticeable. Diffuse râles over both lungs, on the right side pleuritis.



Dispargen having not proved effective,

July 23, 24, and 25, daily 0.2 gm. of argochrome were given intravenously in 20 c.c. of solution. Result entirely negative. Chills continue as heretofore.

Within the next few days a periphlebitic parametric abscess forms on the right side which is drained through a vaginal incision.

Infectious process continues uninfluenced.

Aug. 3, 1918. Exitus.

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P. S., thirty-two years old. Admitted April 27, 1918, died May 3, 1918.

*History.*—Last menses end of January. For past three days uterine hemorrhage, pieces of tissue passing.

*Stat. pres.*—Temperature 38.0° C. Abortion in fourth month. Manual removal of fetus and placenta.

Apr. 30. Icteric discoloration of skin and sclerae. Temp. 40.0° C.

Blood cultures: Streptococci, slightly hemolytic.

Patient received three intravenous injections of 10 c.c. of argosan. No effect on fever or general condition.

Gradually failing, patient died on May 3, 1918.

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K. A., thirty-five years old. Admitted Jan. 20, 1914, died April 3, 1914.

*History.*—On Jan. 11, delivered of twins, first extracted with forceps, second extracted in foot presentation. Manual removal of placenta. Since Jan. 16, fever and chills.

*Stat. pres.*—Temperature 40.4°, chills. Purulent fetid lochia. Second degree perineal laceration. Subinvolution of uterus.

On five successive days patient received one hypodermic injection each of tenosin to hasten involution.

Since temperature continued high with daily chills, and blood cultures are positive for streptococci, from Jan. 30 up to Feb. 8, 10 c.c. of electrocuprol are injected intravenously daily.

No influence on fever or general condition. Daily chills, temperature rising to 41.3° C.

There are no chills for a few days, but fever remains high. Later, again daily chills, at times several times a day.

From Mar. 8 to Mar. 15, daily intravenous injections of 10 c.c. of a 2 per cent solution of electronicke. Effect entirely negative.

With gradual failure exitus on April 3, 1914.

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W. M., twenty-seven years old. Admitted Feb. 18, 1914, died Mar. 9, 1914.

*History.*—Last menses four months ago. Since yesterday hemorrhage with shreds of tissue.

*Stat. pres.*—Abortion in fifth month. Spontaneous expulsion of fetus and placenta.

Two days later temperature up to  $40.3^{\circ}$ , chill. Palpatory findings negative.

Blood culture: Streptococci, slight hemolysis.

From Feb. 25 to Mar. 3, daily intravenous injections of 10 c.c. of a 2 per cent solution of electrocuprol. No reactions but also no effect.

Temperature continued high, several chills.

Patient failed steadily and died on Mar. 9, 1914.

## CHAPTER VII

### CHEMOTHERAPY

#### Aniline Dyes and Their Compounds

Satisfactory experience with the curative influence of certain dyes on malaria, protozoic diseases and spirilloses naturally led to investigations concerning their possible usefulness as well in the treatment of puerperal infections. At the outset, however, it might be remarked that exaggerated hope in this respect hardly seems justified, because there exists a definite affinity between such dyes and the protoplasmatic body of protozoa while nothing is known concerning a similar almost specific relation to bacteria and especially to those predominating in the causation of puerperal infections.

**Argochrome.**—The first therapeutic experiments were made with methylene blue. In the center of interest in this respect stands a combination of this dye with silver (argochrome)<sup>1</sup> prepared by Merck for Edelmann and Mueller, who reported good results from its use. Theoretically the idea underlying this preparation seems sound. The methylene blue readily taken up by the bacteria will act as the vehicle by which the silver is brought into intimate contact with them. In practical tests this expectation did not realize. Neither was there found a reduction to occur in the virulence of the microorganisms nor did the methylene blue act as the expected dependable conveyer of the silver to the bacteria. Already earlier laboratory tests of Huessy had failed to support the claims made for argo-

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<sup>1</sup>A combination of methylene blue with silver nitrate. A brown powder dissolving in water with blue color, containing 20 per cent of silver. Usually employed intravenously in solutions of  $\frac{1}{2}$  to 4 per cent.

chrome. He found that it hardly retarded growth of the culture and that it exerted no influence on the virulence of those bacteria which are more resistant to penetration. The effect in clinical use was equally inconstant. However, some writers reported most gratifying results, e.g., Kuehnelt in 20 cases. Huessy himself, who at first felt rather enthusiastic, was later decidedly more reserved in his opinion concerning this preparation.

Influenced by the most encouraging reports of earlier writers we had employed argochrome but finally had felt greatly disappointed. In order to arrive at a more definite conclusion concerning its value we once more started its use in another series. A few histories will illustrate how little dependable it proved in our hands.

K. W., thirty-four years old. Admitted Jan. 6, 1918, discharged cured Jan. 19, 1918.

*History.*—Last menses end of September. Since Jan. 5 hemorrhage, also fever and chills.

*Stat. pres.*—Seemingly intact pregnancy in second lunar month. No hemorrhage, no fever.

On the two following days temperature rising to 38.4° C. and 30° C. Therefore,

Jan. 10, uterus emptied.

Jan. 11, afebrile.

Jan. 12, chill. Temp. 40.6° C. Intravenously 0.2 gm. argochrome. Blood culture: *Staphylococcus aureus*.

From Jan. 13 to Jan. 19, 1918, patient afebrile. Discharged well.

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J. N., twenty-seven years old. Admitted Jan. 22, 1918, discharged cured Feb. 3, 1918.

*History.*—Last menses Nov. 1, 1917. On Jan. 17, patient claims fetus passed. Since that day vaginal hemorrhage.

*Stat. pres.*—Incomplete abortion in second month.

Jan. 22. Curettage.

Jan. 23. Temp. 40.0° to 41.0° C. Chills. Blood culture: sterile. No local findings.

Jan. 24. Temp. 39.3°. Intravenously 0.2 gm. argochrome.



Jan. 25. Highest temperature 38.3°. Another 0.2 gm. of argo-chrome.

Jan. 26. Afebrile.

Jan. 27. Temperature rising to 39.2° C.

From next day on afebrile until discharge on Feb. 3, 1918.

K. J., twenty-seven years old. Admitted Dec. 21, 1917, died Jan. 14, 1918. (Fig. 12.)

*History.*—Last menses early in September. Eight days before admission abortion, claimed to have been spontaneous. Three days later fever and chills.

*Stat. pres.*—Temperature 38° C. No vaginal hemorrhage. Uterus somewhat enlarged, soft. Adnexa free.

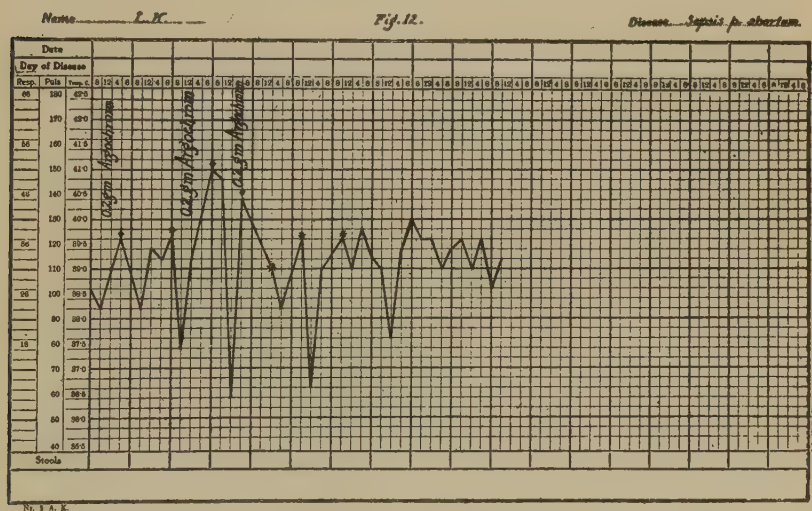


Fig. 12.—Repeated injections of argochrome without any effect.

Dec. 24. Continuous fever up to 40.2°. Blood culture: streptococci, strongly hemolytic. Widal reaction negative.

Dec. 26. Intravenously 0.2 gm. of argochrome. No effect. Fever continues high, chills. Blood culture: streptococci.

Dec. 28 and 29. Each day 0.2 gm. argochrome. Effect nil. Fever and general condition absolutely uninfluenced.

Later an endocarditis, pneumonia and pleurisy developed. Numerous petechia on skin of entire body.

Jan. 14, 1918. Exitus.

H. B. Admitted Dec. 27, 1917, died Dec. 31, 1917.

*History.*—Last menses six weeks ago. Three weeks ago aborted. Eight days ago another hemorrhage. Was curetted. Since that time constant fever and chills.

*Stat. pres.*—Temperature 39° C., pulse 144. Purulent discharge. Cervical canal open. Uterus enlarged and soft. To the right a tender mass, size of hen's egg; in left parametrium an oblong infiltration. Blood culture: streptococci.

Dec. 28 and 30. Intravenously 0.2 gm. of argochrome. No effect.

Dec. 31, 1917. Patient becomes delirious and dies.

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M. P., twenty-four years old. Admitted Jan. 19, 1918, died Mar. 20, 1918.

*History.*—Last menses Oct. 2, 1917. On day of admission fetus was expelled. Fever and chills.

*Stat. pres.*—Complete abortion in third month.

To avoid operative emptying of uterus stypticin was given in attempt to cause spontaneous expulsion of retained placenta. Several injections. No result.

Since hemorrhage continued profusely on Jan. 21, uterus was emptied.

For next two days fever (between 39° and 40° C.). Chills. Blood culture: streptococci.

Jan. 24, 25, and 26. Each day argochrome 0.2 gm. intravenously. Injections well borne.

Jan. 27. Blood culture: sterile. Temperature unchanged.

Jan. 29. Blood culture: streptococci.

During next days a periproctal abscess formed on left buttock. Shortly afterwards abscess was opened; not followed by fall in temperature.

Blood cultures persistently show streptococci.

In the absence of any signs of improvement, with temperatures remaining persistently high, first a trial was made with an intramuscular injection of milk, chiefly to increase by reaction patient's resisting powers. Next day another injection of argochrome. All in vain. Patient gradually sank and died on Mar. 20, 1918.

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B. H., twenty-seven years old. Admitted Mar. 11, 1919, died April 10, 1919. (Fig. 13.)

*History.*—Last menses Dec. 1 to 5, 1918. For last eight days severe genital hemorrhages.

*Stat. pres.*—Uterus enlarged corresponding to a pregnancy of two months, soft. External os closed. No hemorrhage. Adnexa and parametria free.

Since temperature is not high for first few days, no specific therapy employed.

Mar. 13. Several chills, fever above  $39^{\circ}$  C.

Mar. 14. Condition the same. First intravenous injection of 20 c.c. of one per cent solution of argochrome.

Mar. 17. Condition unchanged. Blood culture: streptococci. Another injection of argochrome.

For the next few days no improvement in spite of repeated

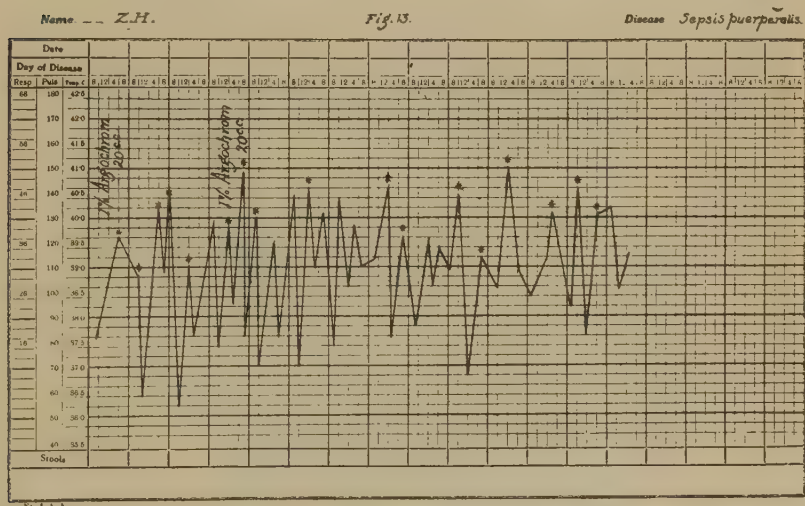


Fig. 13.—Streptococcic sepsis. Icterus. Argochrome injections without effect.

injections of argochrome in same dosage. In left lower lobe of lung pneumonic focus develops (abscess). Pronounced icterus of skin and sclerae.

With gradual deterioration of general condition finally exitus on April 10, 1919.

It seems necessary to emphasize here that also the injections of argochrome and of similar preparations are followed by a marked hyperleucocytosis and to it we ascribe whatever favorable effect might follow such injections.

We used at first from 0.2 to 0.4 gm. of the argochrome

dissolved in 20 or 40 c.c. of distilled water, later resorted to much larger doses but without being able to ascertain that the effect would become either better or more dependable.

Exactly as with several other remedies also in regard to argochrome we finally arrived at the conclusion that good results obtained in treating cases of sepsis of other origin are not necessarily duplicated in instances of puerperal infection. It is the peculiar mode of infection and the characteristic tendency to formation of thrombi in this latter group which interfere both with reliability and degree of action of methylene silver. A few favorable results prove nothing. A definite percentage of cures cannot be calculated not even from a series which includes the less serious cases. However, since the intravenous infusion of the 1 per cent solution is apparently free of all risk to the patient, it might as well be tried, because obviously every remedy at times might be effective. It certainly is not justifiable to entertain exalted hopes.

I warn specifically against subcutaneous or intramuscular injections of argochrome because they are painful and not so rarely result in necrosis and abscess.

Rolly, however, on account of two favorable results he had observed, particularly favors the intramuscular application and thinks that the resulting abscess actually plays a rôle in the obtained cure. In his opinion, the necrotic tissue represents a blood-foreign substance and bacteria possibly are discharged from the blood stream into the newly formed abscess. The method of Rolly from this point of view obviously is then identical with the now antiquated method of the fixation abscess, of which I shall have to say more later on. It might however be pointed out in this connection, that a fixation abscess as a rule is sterile.



**Other Dyes.**—Roosen experimented with divided administration of calomel and methylene blue. Afraid to inject directly a bichloride solution he hoped in this manner to cause the corrosive sublimate to form within the body. The calomel, circulating in the blood, tends to take up chlorine which it could obtain from the methylene blue, which is the chlorate of tetramethylthiamine. He injected first the methylene blue which shows a marked affinity to the germ bodies and will remain attached to them even after it has been dissolved out of other cell structures. If the calomel is introduced later, at a time when a methylene blue residue is left only in the bacteria, the antiseptic sublimate would be formed only in them, while all the other cells in the body would be affected solely by the decidedly less toxic calomel. The best technic for this method of therapy is the following: Within twelve hours, 0.2 gm. of pure methylene blue is given four to six times by mouth. Only twenty-four hours after the last dose, 0.2 gm. of calomel is injected intramuscularly. According to Roosen the method has proved eminently satisfactory during the war in septic wounded soldiers. I am not aware that any similar good results have been reported in regard to cases of puerperal sepsis.

A number of other dyes have been considered valuable as antiseptics and therefore have been employed intravenously in the treatment of puerperal fever, chief among them the aniline dyes, brilliant green, gentian violet, safranin and fuchsin (Bresgen, Stilling and Worthmann). The three dyes, mentioned last, in the hands of Huessy proved more valuable than methylene blue, the others are practically ineffective, eosin and indigocarmin certainly so.

More faith seemingly might be placed in the acridin combinations which used to be employed only in trypanosoma diseases. Acridin-yellow, e.g., was found to inhibit bacterial growth in a dilution of 1 to 80,000. Still more effective proved the acridinium combinations. They prevent the

growth of streptococci in a dilution of 1 to 100,000, and since other bacteria were found to be decidedly more resistant, these compounds were looked upon as being almost specific in their action on streptococci (and also on gonococci?). A silver preparation of acridinium on the market is many times more potent than the dye itself. It interferes with bacterial growth in a dilution as low as 1 to 200,000. It is of very low toxicity and therefore its therapeutic use free of risk. It has the great advantage over argochrome in being nonirritating and never causes abscesses. Huessy reported good results from its early application in 12 cases of sepsis.

The preparation most extensively used at the present time is trypaflavin<sup>2</sup>. First prepared by Benda the substance is now on the market in form of a soluble powder (Casella in Frankfurt). All solutions must be freshly prepared. The usual dose is 0.2 gm. in 20 c.c., or 0.4 gm. in 40 c.c. of distilled water. More recently we have given it in much larger doses without ever having seen stormy reactions. The intravenous injection as a rule is borne well, the symptoms being not more marked or more annoying to the patient than any intravenous injection is. A striking, yellow discoloration of skin and sclerae, proportionate to the amount of the substance injected, appears immediately and, in contrast to the bluish discoloration after argochrome, will persist for several days even if the injection is not repeated. The elimination of the remedy through the kidney is evident for days by the intensely yellowish color of the urine. As a disadvantage of trypaflavin I must mention its tendency to cause extensive thrombosis at the site of injection, probably as frequently as the Pregl solution. Another shortcoming is the likelihood that after repeated, or one large dose, the patient's appetite may remain poor in spite of a marked improve-

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<sup>2</sup>See footnote<sup>2</sup> on page 76.



M. A., nineteen years old. Admitted Oct. 15, 1921, discharged cured Oct. 1921. (Fig. 15.)

*History.*—Last menses Aug. 1, 1921. Claims to be bleeding for past week.

*Stat. pres.*—Icteric discoloration of skin and sclerae. No hemorrhage. Uterus corresponds to pregnancy of two months, soft. External os closed. Adnexa and parametria free.

Oct. 15. Chill in the evening.

Oct. 16. Temperature  $40.2^{\circ}$  C., chill. First intravenous injection of trypaflavin.

Oct. 17. Temp. still high, no chill. Second injection.

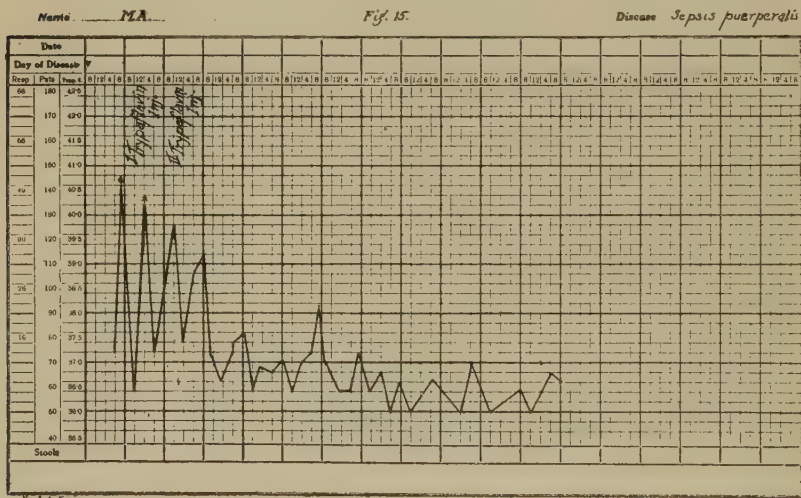


Fig. 15.—Prompt reaction after intravenous injection of trypaflavin.

Oct. 18. Critical fall of temperature.

As a whole patient from then on is afebrile with only occasional slight rise.

Oct. 29, 1921. Discharged cured.

Very severe type of infection with icterus, but good and rather prompt response to trypaflavin.

A. K., thirty-four years old. Admitted Oct. 3, 1921, discharged cured Oct. 22, 1921 (Fig. 16.)

*History.*—On Sept. 23, 1921, spontaneous partus outside of hospital.



Nine days postpartum, a few days after having left bed and resumed household duties, fever and chills.

*Stat. pres.*—Uterus enlarged and soft. Fundus three fingers above symphysis. Adnexa and parametria free.

During next few days intermittent fever. Deep remissions alternate with temperatures up to 40° C. Left-sided parametritis develops.

Oct. 13. Chill. Palpatory findings the same.

Oct. 14. Temperature still high. Trypaflavin injected.

Oct. 15. Critical drop of temperature. Second dose of trypaflavin.

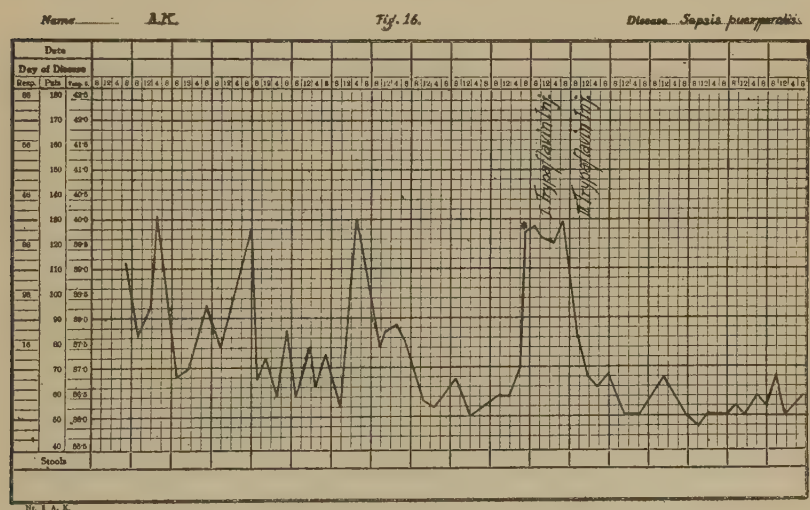


Fig. 16.—Seemingly prompt fall of temperature after trypaflavin in an infection localized in the parametrium. Marked tendency to spontaneous remissions of temperature.

From then on afebrile.

Oct. 22, 1921. Discharged cured.

A light infection with localization in left parametrium. Tendency to spontaneous remissions of temperature. Effect of trypaflavin not certain.

S. I., twenty-seven years old. Admitted Oct. 21, 1922, discharged cured Nov. 15, 1922. (Fig. 17).

*History.*—Three days ago spontaneously delivered outside of hospital. On day before admission temperature rising, two chills.

*Stat. pres.*—Fundus two fingers below navel. Adnexa and parametria free. Gynergen given.

Oct. 26. Temperature above  $39^{\circ}$  C. First intravenous injection of tryptaflavin.

Prompt reaction. Patient is afebrile for next three days.

Oct. 30. Temperature again up to  $39^{\circ}$  C. Chill. Second dose of tryptaflavin.

Nov. 2. Patient afebrile. Blood culture: sterile.

From then on temperature remains normal. At the site of injection a large infiltration forms, which later had to be incised.

Nov. 15, 1922. Patient discharged on her request.

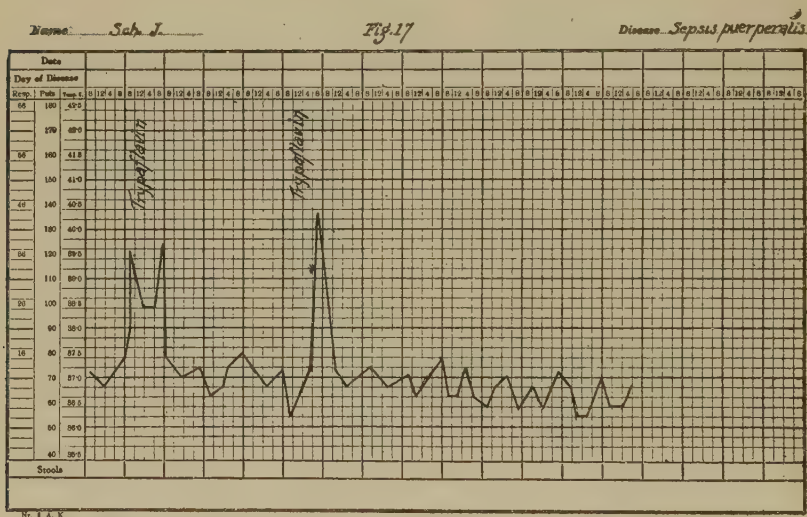


Fig. 17.—Prompt fall of temperature after tryptaflavin.

A relatively light case (blood culture: sterile). Prompt effect of tryptaflavin. Infiltration from injection.

M. W., twenty-five years old. Admitted Feb. 23, 1921, discharged cured May 7, 1921. (Fig. 18.)

*History.*—On Feb. 21, 1921, delivered of twins (first born spontaneously in head presentation, second extracted in breech presentation). Manual removal of placenta outside of hospital. A few hours after delivery high fever with chilly sensations.

*Stat. pres.*—Uterus properly involuted. Region of right uterine adnexa somewhat sensitive to pressure, but no definite resistance. In the evening chill.

First intravenous injection of trypaflavin.

Feb. 26. Condition unchanged. Second dose of trypaflavin.

Feb. 28. No effect. On account of high temperature in evening third injection.

Mar. 3. Chills have ceased but fever remains high. Fourth injection of trypaflavin.

Mar. 5. Evening temperature above  $41^{\circ}$  C., chill. Patient is delirious. Fifth injection.

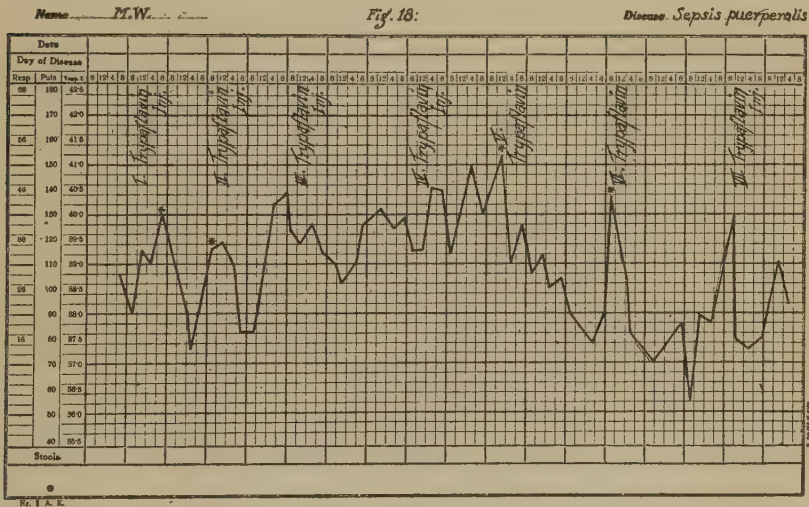


Fig. 18.—Repeated injections of trypaflavin without effect. Recovery probably due to localization of infection in the adnexa.

Mar. 7. Temperature falls to normal.

Mar. 8. New rise. Chill. Sixth injection of trypaflavin.

Mar. 9 and 10. Temperatures low.

Mar. 11. Again rise to  $39.8^{\circ}$  C. Seventh dose of trypaflavin.

During next days occasional remissions, but evening rise of temperature.

Up to Mar. 16, patient received an eighth, ninth, and tenth dose.

Since absolutely no effect could be noticed from these injections, they were discontinued.

The temperature curve (reproduced only in part in Fig. 18)

from then on registered the same picture of intermittent and remitting fever.

Adnexal tumors develop on either side which gradually regress during patient's stay in the hospital.

After many weeks of hospital treatment patient is finally discharged, seemingly well, on May 7, 1921.

The cure cannot be credited to the trypaflavin because the course of the disease, as clearly shown in the temperature chart, was not in the least influenced by the ten injections. The fortunate outcome is solely due to the fact that

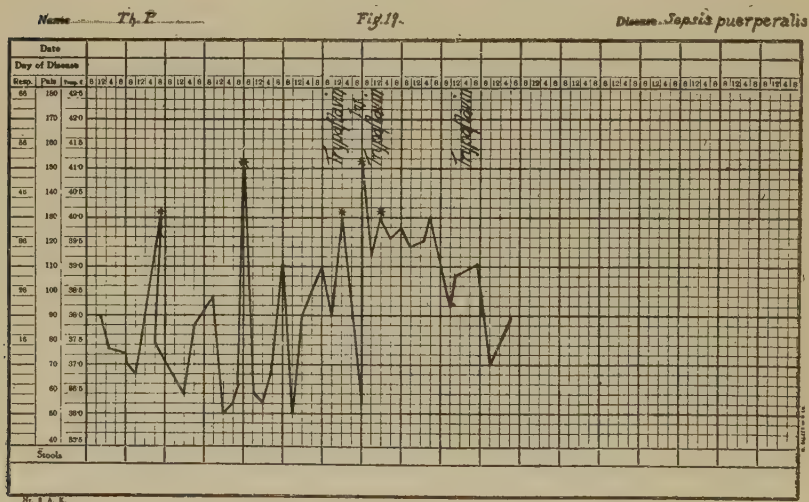


Fig. 19.—Injections of trypaflavin without any result. Peritonitis.

the infection became localized in the adnexa, a circumstance which, as is well known, always betters the prognosis.

T. P., twenty-seven years old. Admitted Nov. 15, 1921, died Nov. 25, 1921. (Fig. 19.)

*History.*—Last menses June 13 to 15, 1921. Claims to have aborted spontaneously on Nov. 14. Same evening fever and chill.

*Stat. pres.*—Uterus enlarged corresponding pregnancy of four months. External os open for one finger. Adnexa and parametria free.



Nov. 16. Moderate hemorrhage. In the evening chill, temperature  $40^{\circ}$  C.

Nov. 18. Severe hemorrhage requires curettage, followed by chill.

Nov. 19 and 20. Temperature elevated ( $39^{\circ}$  C.), but no chill.

Nov. 21. Temperature reaches  $40^{\circ}$  C., chill. First intravenous injection of tryptaflavin.

Nov. 22. Condition unchanged. Second injection, followed by chill.

Nov. 23. Temperature high but no chill. General condition fair.

Nov. 24. Patient complains of abdominal pain and is nauseated. Lower abdomen somewhat distended and tender to pressure. Clinically no signs of peritonitis. Third injection of tryptaflavin.

Nov. 25. Patient complains of severer pain, abdomen diffusely tender. Pulse fast, of low tension. In view of general sepsis it is decided not to operate though the diagnosis of diffuse peritonitis is made. Died same evening.

The injections of tryptaflavin had no effect on temperature or general condition. However, it is impossible to determine what effect the remedy might have had, since the patient succumbed chiefly to the foudroyant peritonitis.

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E. S., twenty-two years old. Admitted May 1, 1921, died May 8, 1921. (Fig. 20.)

*History.*—Last menses end of February. A week ago severe hemorrhage with passing of tissue. Fever for two days.

*Stat. pres.*—Uterus corresponds to pregnancy of two months, soft. Cervix patent. Adnexa and parametria free.

By means of curettage a good deal of retained placental tissue is removed.

May 3. Temperature continuously high. No chills. Tryptaflavin.

May 4. Temperature still high. Moist râles in lower lobes of lungs on both sides. Second injection of tryptaflavin. Blood culture: streptococci.

May 5, 6, and 7, daily injections of tryptaflavin. Absolutely no effect.

May 8, 1921. Exitus.

Very acute case with quick formation of metastases in lungs. Also renal abscesses. Tryptaflavin in this case of-

fered no more chance than would any other medication. No leucocytic reaction.

L. B., nineteen years old. Admitted April 19, 1921, died May 5, 1921. (Fig. 21.)

*History.*—Last menstruation on Jan. 28. On April 15, hemorrhage, claimed to have started spontaneously. Next day a piece of "meat" had passed. Cured before admission. Since then fever, chills and abdominal pain.

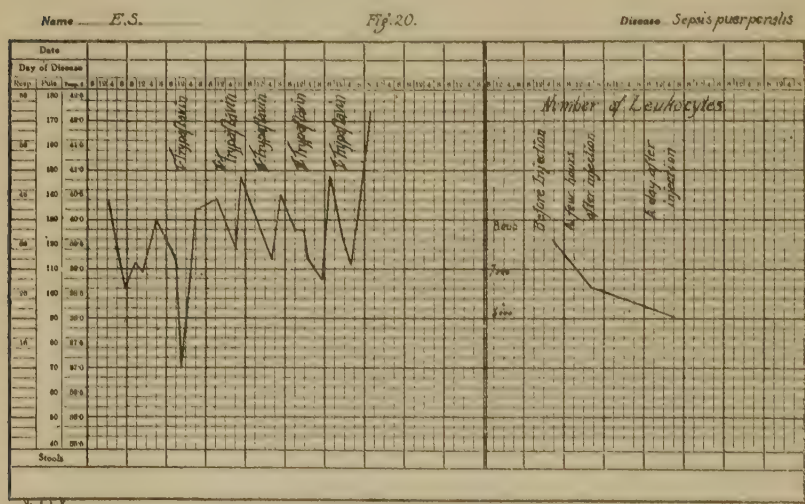


Fig. 20.—Trypaflavin injected daily for five days without any effect. Leucocytic curve corresponds to unfavorable prognosis.

*Stat. pres.*—Uterus enlarged, soft, anteverted. Adnexa and parametria free.

April 21. Temperature continuously high. Chill. First injection of trypaflavin.

Apr. 23. No reaction. Blood culture: anærobic streptococci in pure culture.

During next few days almost daily an injection of trypaflavin, but without visible effect. Daily chills, temperature continues high. Severe icterus developed and she failed gradually, became paralyzed on right side of body and expired on May 5, 1921.

Very severe anaerobic infection with extensive thrombosis of pelvic veins. An embolic encephalomalacia hastens the end.

J. H., twenty-one years old. Admitted Mar. 18, 1921, died Mar. 27, 1921. (Fig. 22.)

*History.*—Last menses end of January. On Mar. 15, curetted outside of hospital. Since then fever and chills.

*Stat. pres.*—Uterus somewhat enlarged and soft. To the left of uterus an irregular, tender, oblong infiltration about thickness of two fingers. Metrophlebitis.

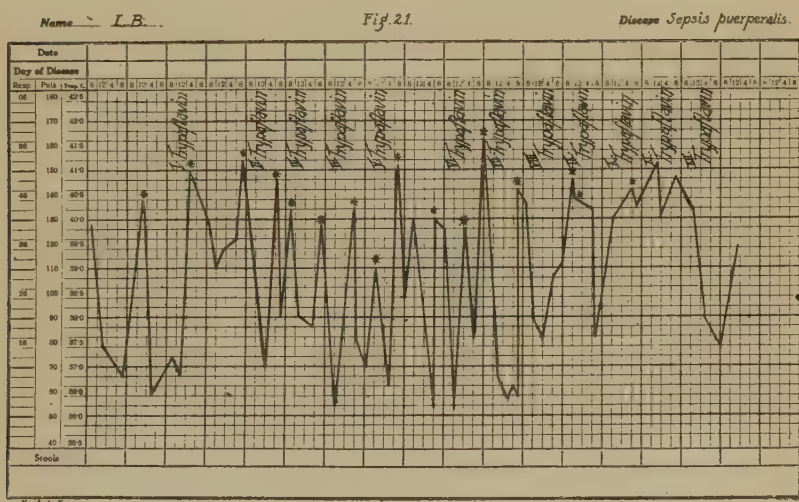


Fig. 21.—Injections of trypaflavin given daily without any effect. Anaerobic infection.

Mar. 19. First injection of trypaflavin.

Mar. 22. Temperature unchanged. Second injection.

Mar. 25. Condition unchanged. Infiltration to the left increased. Vaginal incision. Escape of small quantity of blood and pus. Cultures from pus and blood. Both show "small" streptococci. (We designate in this manner a special type of streptococci which we have discovered in a number of our cases. The individual coccus is only about one-fourth the size of the typical streptococcus. Otherwise in regard to the formation of chains, growth on various culture media, etc., we cannot find





of high concentration, especially in the report of Stejskal. I refer those interested in the rationale of this procedure (osmosis, changes in blood concentration, resulting increased efficiency of infused substances, etc.) to this paper. We thought it possible that the sugar might stimulate the formation of antibodies and other protective substances which would support the action of the dye, and also hoped that the large amount of sugar might produce an effect similar to that of a foreign protein. Two very seriously sick patients treated in this manner actually recovered, but in view of the small number and the ever present possibility of mere coincidence, we shall draw no conclusions from these observations. In the meantime Latzel has dealt with this same problem though not specifically in relation to puerperal sepsis.

Argoflavin represents a combination of silver nitrate with trypaflavin, containing approximately 20 per cent of silver. It is administered intravenously in a half per cent solution in doses of 0.1 to 0.2 gm. Occasionally it causes thrombosis at the site of injection. We have no extensive personal experience with this preparation, but literature contains several favorable reports (Leschke, Bohland).

The most recent preparation of this group is rivanol.<sup>1</sup> In gynecology it was first employed chiefly only in the treatment of peritonitis, especially on account of its seeming value in the therapy of localized suppurations (phlegmons, mastitic abscess).

Its specific value for such conditions is based on the fact that its antiseptic power remains unimpaired by the presence of pus cells. (Morgenroth). Observations so far recorded are limited in number, and final judgment will have to be passed on rivanol at a later date. As a rule 30 to 50 c.c. of a 1 to 1000 solution are injected intravenously.

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<sup>1</sup>See footnote<sup>4</sup> on page 76.

### Arsenic Preparations

**Atoxyl, Arsacetin, etc.**—When atoxyl<sup>1</sup> and arsacetin,<sup>2</sup> prepared by Ehrlich in 1909, had proved themselves valuable arsenic preparations which are well borne by the patients, with comparatively little risk in doses sufficiently large to procure the expected bactericidal effect, gynecologists soon began to experiment with these and similar substances in the therapy of puerperal infections. Again it was thought that special benefit might be derived from a combination of the arsenic with silver which is enjoying a sort of real reputation as a specific for puerperal infections. It was hoped that the addition of arsenic would increase the antiseptic power of the silver, would retard its elimination and thus prolongate its beneficial effect. On theoretical considerations of this sort is based Blumental's silver atoxyl.<sup>3</sup> He ascribed to this preparation the particular advantage that the slow solubility of the silver salt reduced the toxic effect of the arsenic to such an extent that larger and thus decidedly more adequate doses can be administered. Some observers confirmed the gratifying clinical results reported by Blumental. Eisenberg, e.g., described a case of sepsis in the fifth month of pregnancy. A few days after the injection an abscess formed in the kidney region. After its incision patient recovered. Eisenberg explains the development of the abscess as due to the exquisitely chemotactic action of the silver atoxyl which indeed forms an important factor in its curative effect. I cannot quite agree with this view. The abscess formation does prove the leucotactic effect of silver salts but does not prove it to be a fixation abscess because in our very

<sup>1</sup>Sodium paraphenylarsenate. A white powder, soluble in water, containing 24.5 per cent of arsenic. At times it causes disagreeable symptoms such as headaches, gastric discomfort, renal or bladder irritation, paresthesias, collapse, also serious visual disturbances even with permanent blindness. Solutions always must be prepared immediately before use. Fractioned sterilization at low temperatures is necessary.

<sup>2</sup>The acetylate of atoxyl. Curative effect, dosage and by-effects approximately the same as those of atoxyl.

<sup>3</sup>A monosilver salt of amidophenylarsenic acid. It contains 23 per cent of arsenic and 33 per cent of silver.

extensive experience with various metal salts we hardly ever saw a true fixation abscess develop. More likely such an abscess at the site of injection actually represents only a natural reaction to the local destruction of tissues by the arsen-silver salt.

Experimental investigations, among which I might refer to those of Heimann, yielded decidedly less satisfactory results. He came to the final conclusion that it is futile to use these preparations on patients. Similarly negative were the results obtained by Kirchhoff in experiments on animals. He warns against the clinical use of argotoxyl on account of both its toxicity and its marked tendency to cause abscess formation at the point of injection.

A few years ago I tried argotoxyl on two patients but never afterwards, since I failed to notice the slightest beneficial effect. But an abscess forming in each of the two cases from the injection greatly harassed the already weakened patient. For this reason I cannot recommend its use.

**Salvarsan.**—The literature of the past few years no longer contains any reports concerning the use of salvarsan in the therapy of puerperal infections. Some time ago several writers had published glowing reports which, however, did not stand up well under critical review. As a matter of fact one is today surprised with how little judgment some authors could have dared to recommend broadcast the employment of so dangerous a drug with practically no proof that it is of any value. Halle, e.g., described the following observation: An epileptic woman, four days after spontaneous delivery, had fever without chill. "All therapeutic measures, including intravenous injections of collargol, having proved ineffective 0.3 gm. of salvarsan was given. Next day patient was afebrile. Eight days later again rise of temperature. A second dose of 0.3 gm. of salvarsan brought temperature permanently down to

normal." Or Bleyne states that at times the result of salvarsan is very good. Temperature, pulse and general condition become better. Out of four cases treated by him in this manner two died. Also Orlovius in 16 cases had a mortality of 50 per cent. In Halle's case the recovery more likely has nothing to do with the salvarsan. In other cases, though only few in number, a recovery rate of 50 per cent is not particularly encouraging, since it is observed likewise with other therapy and probably as well without any therapy.

As early as 1911 and 1912 we experimented with the original salvarsan using it with all the necessary precautions in the largest permissible doses. Our failure was so decided that we did not even publish our results, but incidentally I have referred to this fact in a little paper of mine dealing with bacterium coli sepsis (published in 1912).

D. A., thirty-four years old. Admitted June 13, 1912, died July 6, 1912.

*History.*—On May 25 normal spontaneous delivery. Afebrile for first few days postpartum. Since seventh day daily high fever with chill. No other subjective symptoms.

*Stat. pres.*—No hemorrhage, no fever. Uterus well involuted, fundus two fingers above symphysis.

June 14. Temperature up to  $41.2^{\circ}$  C. two chills. Blood culture: hemolytic streptococcus. From the uterine secretions grow nonhemolytic streptococci.

Several chills daily, therefore, on

June 26, intravenously 0.4 gm. of salvarsan. No immediate discomfort.

During next two days temperatures lower ( $39.5^{\circ}$  C.), no chills.

July 1. During past few days chills. Intravenously 0.2 gm. of salvarsan.

Effect nil. Daily chills.

July 6, 1912. Patient died.

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M. L., thirty-one years old. Admitted Aug. 12, 1912, died Oct. 20, 1912. (Fig. 23).

*History.*—Nothing of significance in family and past history. Menarche at age of nineteen. Menses regular, four weekly, last-



ting three days, medium flow, no discomfort. Three normal labors. Last menstruation three months ago. Aborted 8 days ago. After that high fever.

*Stat. pres.*—Temperature  $36.6^{\circ}$  C., pulse 84. Vaginal hemorrhage. Cervix soft, canal open for finger. Uterus about the size of a pregnancy of two months, retroflexed, Adnexa free. No other abnormal palpatory findings.

*Diagnosis.*—Incomplete abortion.

With curette only small particles of placental tissue removed. After operation patient had a chill.

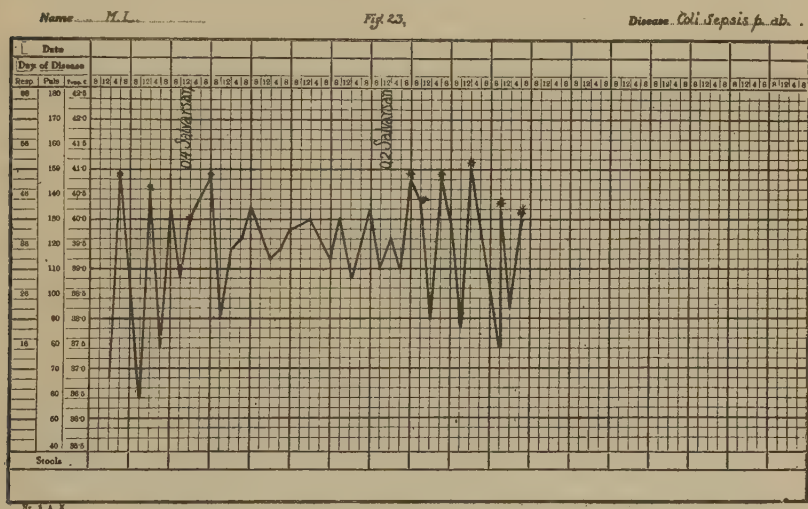


Fig. 23.—Intravenous salvarsan injections. After first injection temporary cessation of chills. Otherwise temperature and course of disease remain uninfluenced.

Vaginal and cervical smears show a few cocci, very many short bacilli, staining Gram-negative, resembling bacterium coli.

Cultures (blood serum, agar and bouillon): pure growth of short, Gram-negative bacilli. Same result from blood culture.

Differential diagnostic investigations made later confirm that it is, as suspected, a bacterium coli infection.

On next day temperature  $39^{\circ}$ , pulse 124, of good tension. Abdomen not tender, soft. Slight bloody vaginal discharge. Uterus retroflexed, enlarged and soft. On the left, an oblong, tender, round infiltration, thickness of little finger, stretching from left edge of uterus towards lateral pelvic wall (metrophlebitis sinistra).

Aug. 14. Another chill (40° C.).

Aug. 15. Intravenously 0.4 gm. of salvarsan. No reaction.

During next days high temperatures but no chills. Bacteriological blood findings unchanged.

Aug. 20. Another chill. Another injection of 0.2 gm. of salvarsan.

No influence on chills. Within the next 6 days a total of 8 chills with temperatures up to 41°. Blood cultures unchanged.

With fever continuing and occasional chills within the next two weeks both parametria develop a hard infiltration. Metrophlebitis unchanged. Metastatic process in right lung.

Sept. 6. A third injection of salvarsan (0.2 gm.).

During next few weeks no noticeable change in temperatures, but there are no more chills.

Blood cultures continue to show pure growth of bacterium coli.

Pulmonary process improving.

Oct. 11. Severe abdominal pain. Abdomen is distended and tender. Both lateral vaginal fornices pushed down by parametric tumors which had developed in meantime.

Patient gradually sinks, sensorium becomes clouded, temperatures lower as result of collapse.

On Oct. 15, metastatic abscess formed in right parotid (size of pigeon egg). It gradually enlarged up to patient's death on Oct. 20, 1912.

*Autopsy Findings.*—Abscess in right parotid. Heart small, flabby. Small amount of clear fluid in pericardium. Lungs adherent on both sides, upper lobes fairly anemic, lower lobes especially on right side hyperemic. Diffuse purulent peritonitis. Lower half of spleen contains a cavity, lined with ragged spleen tissue, communicating with a large, walled off, abscess cavity. Spleen enlarged to three times normal size. Upper, preserved portion, is hyperemic, dark red, soft, wall of colon at splenic flexure perforated by an ulcer about 4 cm. in diameter, fecal matter entering the abscess cavity. Thick layer of exudate covers anterior and posterior surface of left lobe of liver and also anterior aspect of contracted stomach. Liver small and soft. Gall bladder filled with stones. Kidneys soft, cortex yellow-greyish, medulla pale. Mucosa of urinary bladder injected. Above left ureteral opening a large ulcer with partial suppuration of bladder wall.

Uterus and adnexa adherent to sigmoid flexure. In this manner a cavity is formed lined by fringy, almost black tissue, filled with fetid pus. Left broad ligament taken up into this sac so that the pus at this place reaches the bladder wall. Uterus and vagina as well as right adnexa show only unimportant pathologic

changes. Left ovary is size of a plum, riddled with small thin walled abscesses. Left tube swollen, contains thick greenish pus.

From heart blood, peritoneal pus and parotic abscess bacterium coli grown in pure cultures.

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I wish to emphasize that we did not resort to salvarsan in Ehrlich's sense of a *therapia sterilisans magna* but simply counted on an increased arsenic effect and a stimulated antibody reaction through greater activity of the bone marrow.

In the five cases we treated with salvarsan we could occasionally notice a reduction in the occurrence of the chills and a slight leucocytosis. This was the sum total of the achieved result since all five patients died.

Neosalvarsan I shall discuss in a subsequent chapter.

### Leucostimulants

The leucocytes play the leading rôle in the modern doctrine of immunity, and Metschnikoff in particular considers them the main carriers of the immune bodies (alexins). Therefore for some time now an attempt has been made to strengthen the resistance of the body against invading bacteria by increasing the number of leucocytes and by augmenting the avidity with which they attack the bacteria. Experiments, heretofore only empirical, were placed on an exact scientific basis by the report, prepared for the German Surgical Congress of 1904 by v. Mickulicz and Miyake, on increased resistance resulting from hyperleucocytosis. These investigations later were carried on by Renner and published in an exhaustive paper.

As demonstrated in preceding chapters, the beneficial effect of most of the already discussed therapeutic procedures of puerperal infections, at least in part, depends upon a more or less marked increase in the number of white

cells in the blood. Nucleinic acid always appears in these experiments as the leucostimulant of particular value.

**Nucleinic Acid.**—Mickulicz and Miyake injected nucleinic acid subcutaneously in doses of 50 c.c, or administered it *per os* 5 to 6 gm. every twelve to twenty-four hours, adding a saline infusion, until sensitiveness of the long bones manifested itself. It is assumed that this tenderness of the bones indicates the prompt substitution of the erythrocytes destroyed by the infection, and the beginning of the hyperleucocytosis. The saline solution is supposed to dilute the toxins in the blood, to further circulation of the body fluids, and moreover to prove advantageous because the alexins are fully active only in the presence of neutral salts (Hofbauer).

As a matter of fact at first a temporary hypoleucocytosis appears, which is followed by a pronounced hyperleucocytosis, but the latter decreases soon and usually has disappeared within a few days.

Originally this method of artificial hyperleucocytosis was employed only by surgeons and then solely as a prophylactic measure, especially since Busse had recognized in the postoperative hyperleucocytosis a protective element against infection. The method later was discarded when it was found impossible to ascertain any noteworthy difference in the postoperative course of patients treated in this manner from others. Great discrepancy of views is exhibited in the literature. We find most enthusiastic advocates, like Hofbauer, Hannes, Kroemer or Pollak, and again others who deny the procedure even the slightest value, as, e.g., Kroenig, Pankow, Brunner or v. Graff.

Since 1922 Hofbauer combines in the treatment of puerperal infections the administration of nucleinic acid with intravenous injection of hypophyseal extract and offers the following explanation for the better action of this combination: Even physiologically during labor the leucocytes



increase in number. This is the result of the entrance of hypophyseal hormones into the body fluids. The injection of hypophyseal extract will further stimulate the tissues which produce the antibodies in the hematopoietic system (Borchardt) and which already are energized by hypophyseal hormones during labor. The pituitary extract incidentally also increases the tonus of the uterine muscle and thus through compression of blood- and lymph channels the ingress of more bacteria into the system is impeded.

This theory of Hofbauer undeniably sounds attractive. It actually includes all the desiderata of an ideal therapy of puerperal infection, but it seems rather doubtful that in practice this combination actually fulfills all these expectations. However, I cannot pass definite judgment on it from any personal observations. I have lived through at least a part of the nucleinic acid area, have never seen any good results but still remember the suffering of the patients who invariably developed abscesses at the site of every injection. It was this experience which induced us to discontinue nucleinic acid and kept us from ever testing its combination with hypophyseal extracts. My skepticism in this respect is based as well on other considerations.

When dealing with general therapy in a preceding chapter I mentioned that we favor pituitrin both as a cardiac stimulant and a uterine tonic and therefore we always used it in the septic patients when administering any of the antiseptics (silver preparations, tryptaflavin, etc.). These antiseptics all act as leucostimulants and thus we would be justified in expecting that our own combination in practice should have proved an equivalent to that proposed by Hofbauer. We saw no satisfactory results from it. We have failed to see that the addition of hypophyseal extract in any way improved the effect of the antiseptics.

Also in respect to Hofbauer's assumption that an increased uterine tonicity exerts a beneficial influence our

own observations do not coincide with his. We all appreciate the value of pituitary extract in causing a prompt contraction of the uterine muscle, but we also know the relative brevity of this effect and fear the usual subsequent relaxation. For this very reason we make it our practice to fortify the prompt but fleeting effect of pituitrin on the atonic uterus by the addition of one of the various ergot preparations. Thus we can see that not even the sensitized uterus, during labor or immediately afterwards, reacts to pituitrin entirely in Hofbauer's sense, still less than the puerperal uterus which naturally has lost some of this sensitization acquired during labor. This part of the total effect, looked for by Hofbauer, beyond doubt can more reliably be obtained by means of such remedies as secacornin, gynergen, tenosin, etc. But although their effect is more lasting than that of pituitary extract they cannot achieve what Hofbauer expects, because a compression of blood- and lymph vessels sufficient to preclude a further passage of bacteria through them cannot be procured with any of the known uterine stimulants. As established by the failure of vessel ligatures, not even this procedure can accomplish this purpose.

All that a stimulant of the uterus can do is to cause a forced contraction so that blood or secretions will be unable to collect in larger amounts within its cavity. This reduces for the bacteria within the uterus the chances to multiply and indirectly thus likewise the opportunity to enter in large numbers into the vessels. Of course, those of them that already have entered vessels can be stopped from further progress solely by protective antibodies which impair their vitality or actually destroy them.

These are the main reasons why we do not favor the treatment with nucleinic acid and have never experimented with Rosenberg's phagocytin or with injection of iodine

trichloride, recommended by Kocher and Travel, substances supposed to act in the same manner.

**Fixation Abscess.**—Since the artificial production of abscesses represents a method chiefly dependent upon the effect of a superinduced hyperleucocytosis, we have to deal with this procedure in this connection, although the resulting increase in the leucocytes on the whole is more local than general.

After extensive experimentation with injections of quinine, argentum nitricum and turpentine, the last mentioned substance has finally proved the most reliable for the purpose of producing a fixation abscess. Turpentine as compared with other agents will admittedly cause the formation of an abscess in the largest percentage of instances. Personally I have had more experience with quinine, because we have employed this drug for several years now in many cases to start or to strengthen labor pains. As a rule the injections were given intramuscularly, but often enough with too short a needle or by unskilled hands, to be actually subcutaneous. Abscesses we observed only as the rare exceptions.

Turpentine has been employed therapeutically for a long time, and in fact was advocated for the first time by Brenan of London in 1814. Its use was forgotten when Fochier of Paris in 1883 reintroduced it into the treatment of puerperal fever for the systematic production of so-called fixation abscesses. This writer should be properly regarded as the creator of the turpentine therapy in its modern sense. In Germany and Austria this method found only few followers.

The abscess is produced by the strictly subcutaneous injection of 2 to 5 c.c. of chemically pure, but old, turpentine on the anterior outer surface of the thigh or laterally on the thorax or abdomen.

It must be emphasized here how very important its

exactly subcutaneous injection is, since recent experience with its extensive use in the treatment of adnexal inflammations amply proved that the abscess will fail to appear if the turpentine is injected in such a manner that it is deposited closely over the surface of a bone. A very detailed description of technic of application and subsequent phenomena will be found in the paper of Bardenheuer. Immediately after the injection local redness, edema and swelling are noticed, soon also necrosis of the tissues which came into direct contact with the turpentine. About 16 to 18 hours after the injection there is a small-cell infiltration soon followed by a typical pus infiltration with emigrated leucocytes in enormous numbers. Granulation tissue forms around the necrotic area which reaches the height of its development on the third day. In the course of three to four days the formation of a fluctuating abscess is accomplished.

The amount of pus at times is excessive, 500 c.c. and more. The abscess should be emptied, not before the seventh or eighth day, by mere incision without drainage. Bier's suction hyperemia might now be applied. It is permissible to wash the abscess cavity with sterile water or peroxide. A sterile dressing is applied to prevent secondary infection. The healing process is slow. If the first symptoms, e.g., reddening, do not appear within a few hours, the injection may be repeated.

Many writers claim that the failure of any reaction after a properly administered turpentine injection should be looked upon as an unfavorable prognostic sign. If the fixation abscess forms, the recovery of the patient is not by any means certain, but it is probable. Prognostically most favorable is considered an abscess which shows a tendency towards phlegmonous extension. In the opinion of Voiturier this positively indicates that the patient will recover.



It is not entirely clear just how the various authors account for the curative effect of the fixation abscess. It is certain that the injection will attract leucocytes in large numbers, it is less certain, however, that this accumulation of white cells necessarily also draws bacteria out of the blood stream into this focus, since these abscesses as a rule are sterile and also histologic microscopic study fails to reveal dead bacteria within them. The assumption of some authors that there occurs a chemical transformation or destruction of toxins within these pus cavities, seems as improbable as the supposition of others that some sort of general systemic effect checks further growth of the bacteria in the blood.

Therefore the conclusion seems inevitable that the turpentine injection or fixation abscess leads only to a moderate hyperleucocytosis and thus to a slight increase of the phagocytic index, results which can be procured in a more reliable and simpler manner by other procedures.

It appears unlikely that the turpentine by itself exhibits an extensive general antiseptic power and therefore it is not reasonable to suppose as, e.g., Fabre does, that turpentine exerts a specific action on streptococci.

According to present views (Luithlen), the occasional beneficial effect of the substance is best explained in the following manner: At the site where the turpentine was deposited, tissues become necrotic. Thus protein split products are formed. The resorption of these blood-foreign substances affects the body in the sense of a parenteral introduction of body-foreign proteins such as milk or vaccines. The method of producing large fixation abscesses in its last analysis represents only foreign-protein therapy.

If laboratory experiments actually establish a growth-retarding action of turpentine in the test tube, this fact proves nothing for its usefulness in a case of systemic infection for the various reasons I have mentioned on several

occasions in preceding chapters. Whether administered by means of a subcutaneous injection or applied to a wound surface, turpentine could develop only a strictly local antiseptic effect.

In this last-mentioned manner it actually has been advocated by some French obstetricians, especially prophylactically. A stock emulsion is prepared by mixing 300 gm. of turpentine with 600 c.c. of sterile distilled water and 5 gm. of tinct. lign. panam. Immediately after expulsion of the placenta 30 c.c. of this stock solution diluted in 1000 c.c. of sterile water, heated to 40° C., are injected into the uterus. The resulting thorough impregnation of the entire birth channel with turpentine is supposed to be evidenced by the characteristic odor of the lochia which persists for two or three days.

The intrauterine application of the solution, in serious infections strengthened by the addition of pure turpentine, has been recommended also for curative purposes. It moreover has been suggested to treat puerperal infections by means of subcutaneous infusions, given twice daily, of a solution containing one gram each of oil of turpentine and of spiritus vini in 200 c.c. of sterile saline.

Among German obstetricians especially, Cramer favors this local treatment of the entire birth channel with a turpentine solution and emphasizes as its chief advantage that the disinfectant effect actually continues for days. Since turpentine, he states, has no escharotic effect, secretions are not retained underneath crusts forming with other antiseptics, and since its resorption is slow, signs of general intoxication or of renal irritation are never observed. Cramer asserts that turpentine used in this manner eliminates all the dangers incident to operative evacuation of the septic uterine cavity as is evidenced by the fact that as a rule it prevents the customary chill following the operation.

However, this method has not met with general approval either.

Like all German obstetricians we also had but little opportunity to acquire extensive personal experience with the therapy of fixation abscesses. We have attempted now and then to produce artificial abscesses, not always successfully, but have never felt any inclination to study the question systematically on a large series. Theoretical arguments against the possible value of the method and a few disagreeable incidents in practice account for our own hesitation. We had no reason to look for a beneficial general effect and had no faith in the local action. The one favorable feature of the procedure, the hyperleucocytosis, we can procure by methods decidedly simpler and less troublesome to the patient. We fear that sole resort to the fixation abscess without any other therapeutic effort may involve the loss of valuable time to the great disadvantage of the patient.

The results in a few cases in which we combined the turpentine therapy with other forms of treatment could not change our opinion of a method which appears so little in harmony with our modern conception of what constitutes an appropriate fight against a systemic infection.

### Protein Therapy

**Bacteriotherapy (Vaccines).**—The extraordinary prophylactic value of vaccination against smallpox and the not less significant results obtained with passive immunization against tetanus, diphtheria, and other infectious diseases, opened the way for the propitious development also of an immunotherapy. The first steps in this direction were taken by Wright and his followers, who were able to report imposing results from bacteriotherapy in staphylococcosis, and who had based such a therapy on a fully scientific basis by clearing up several essential features of the immunity

problem, as, e.g., the existence of a negative phase. They also had worked out certain important technical details. For a time it seemed that extravagant hopes, at least in regard to the successful treatment of such diseases as typhoid and staphylococci infections, finally had been fully satisfied. But as soon as the attempt was made to apply these newer achievements likewise to the treatment of puerperal fever, early enthusiasm was quickly followed by bitter disappointment.

Purely theoretical investigations, will say in regard to the opsonic index of patients suffering from puerperal fever, yielded results which readily proved that its determination is actually of no value for bacteriotherapy. It would lead us too far to enter here into a consideration of these problems. They are discussed in detail in all textbooks of serology and in a few papers more specifically dealing with puerperal infections (Schiffmann and Kohn, Heynemann, or Bine and Lissner). I will merely state that all authorities soon concurred in the opinion that the practical application of this principle of the opsonic index is greatly interfered with, if not rendered useless, by the great technical difficulty of its determination and by its evident variability also in normal healthy individuals.

For this reason I feel that the enthusiasm shown by some American writers in the problem of immune opsonins is rather out of proportion to their practical clinical utility.

However, these investigations did prove conclusively that the negative phase must be duly respected and that during it, which is during the first two days after an injection, any second injection is better avoided, that it is safer practice to delay the second injection to the fourth or fifth day.

Views in favor of autovaccinotherapy have been expressed by several English and American gynecologists (Blair Bell, Murray, James, Montgomery, Goodall, etc.).



Noteworthy of special mention is the view of Gow, opposed to the generally prevailing opinion, that the autovaccine preferably is prepared from a culture secured through a uterine smear and not, as is customary, from a positive blood culture.

Studies both on man and animal have established the advantage of autovaccines over the first employed standard vaccines which in the beginning, in analogy to the sera used in serotherapy, had been prepared by mixing vaccines of different origin, so-called polyvalent mixed vaccines. Thus some writers had recommended a vaccine for puerperal fever which was polyvalent in the sense that it represented a mixture of all those bacteria which most commonly are causing puerperal infections, namely strains of streptococci, staphylococci and bacterium coli (Hawlyard, Wolverton).

However the recognized inferiority of standard vaccines over autovaccines offered a new obstacle to the popularization and propagation of this immunization therapy. The preparation of autovaccines represents definite technical difficulties and requires time. The standard vaccine at least could be procured readily from the nearest drug store. To procure the necessary discharge and instruct a pathologic laboratory to prepare an autovaccine is a cumbersome procedure for the practitioner. It furthermore is a procedure that renders this particular therapeutic method applicable only to more chronic cases. They are naturally the milder cases of infections which very often recover spontaneously. And it is due to this fact that it became so difficult to arrive at a precise opinion concerning the curative value of vaccinotherapy. Autovaccines never have been used to any extent in the truly dangerous acute cases that bear no delay in treatment. Some writers tried to avoid this evident shortcoming by employing the so-called simultaneous method, administering the corresponding serum

until the autovaccine was ready for use. This might be good practice but final results then again prove nothing for or against the value of vaccinothrapy (Watters and Eaton, Bailey, Murray, Bumm's clinic). Some obstetricians actually prefer this combination of serum and vaccine (Levy and Hamm, Schereminsky, Rowlette). That this combination involves the great risk of a possible aggressin effect was pointed out both by Menzer and Heynemann.

Whenever all external difficulties could be overcome, noteworthy results in fact were obtained at least in instances of staphylococcic infections. Conditions, however, are much less favorable in relation to the problem, in which we are interested, namely the treatment of puerperal infections. Here we deal as a rule with a streptococcic infection for which vaccinothrapy never has been found of worth while value.

But another notable step forward in the understanding of this complex problem was made with the introduction of the heterovaccines into therapy. In the beginning of the ninth decade of the past century the first cautious trials were made in this direction, at that time simply on empirical grounds without any scientific justification. Rumpf, in 1892, treated typhoid fever with injections of dead pyocyaneus cultures. Later, in 1911, Renaud reported his striking results in the treatment of such different diseases as peritonitis, phlegmon, cystitis or salpingitis by means of the typhoid vaccine. Others failed to duplicate these results (Kraus, Buswell and Presser).

This seemingly paradoxical effect finally found its satisfactory explanation by the work of Friedberger, Pfeiffer, Foas and Agazotti, Isaëff, and many others. They demonstrated that the parenteral introduction of certain poisons and even of heteroproteins results in a nonspecific reaction of the entire organism and thus in a nonspecific but actual increase of the resistance to bacterial invasion.

Weichardt, R. Mueller, and R. Schmidt observed this identical phenomenon after the parenteral introduction of protein-split products and of proteinlike colloids, the last mentioned, of milk. They established the fact that the injection of these and similar substances, especially directly into veins, will lead to a general reaction which might be sufficient to cause a local or general infection to be cured. Thus the entire process was cleared of all its surrounding mystery and definitely recognized as a systemic reaction to protein, as a phenomenon resembling anaphylaxis, but not identical with it.

Heterovaccination found its extensive and most useful practical application during the war in the treatment of infections of all kind, including typhoid and dysentery, and so it is only natural that it soon was accepted also as a welcome addition to the therapy of puerperal infections.

The results (Kraus, Mazza, Werner and Koehler), though not by any means uniformly gratifying, are such that they must be regarded as very satisfactory at least in comparison to the little that is achieved with any other type of treatment of puerperal infections. Kraus and Mazza injected cultures of bacterium coli, killed with ether, beginning with a dose of 25 million bacteria to one cubic centimeter but soon increasing it to 100 million per injection. Cardiac and renal lesions are accepted as strict contraindications. Werner used the coli vaccine of Kraus and Mazza and another vaccine prepared by the Serum Institute of Vienna, and saw 72 per cent of his cases recover; however, they all had negative blood cultures. In a discussion of Werner's paper before the Vienna Gynecological Society, in 1915, I stated that our own experience rather supports his claims. But continued use forces us to modify this view at the present time slightly in disfavor of the method. The total result apparently is not markedly different from that obtained with any other therapy.

We employed various vaccines, prepared from typhoid, cholera, dysentery, bacterium coli, gonococcus, staphylococcus and streptococcus. One of the streptococcus vaccines was obtained from a large number of different streptococcic strains cultured from several puerperal sepsis cases. At first we dared not give more than a few millions of dead germs, later we increased the dosage to one hundred, two hundred and many more hundred millions, as is the more customary dose of late. Only a few authors still prefer the smaller doses (Schereminsky, Dastler).

The reaction after intravenous injection of vaccines is not different from that of other agents, e.g., metal colloids. The injection itself as a rule is borne well, though there might be slight dizziness, scintillations or a temporary sensation of oppression. Only later, somewhere between one-half and four hours, the temperature begins to rise, up to 40° or above, usually with marked chilly sensation. Within a few hours, especially in a prognostically favorable reaction, the temperature falls critically and then remains at the normal level. In cases with a less hopeful outlook the temperature comes down slowly and may not quite reach normal. Only exceptionally can one expect a permanent result, i.e., continued afebrility, from only one injection. Usually sooner or later the fever again will appear, requiring a second injection followed by the same reaction. Some patients undeniably, after one or more injections, finally recover but unfortunately the majority remain uninfluenced from a therapeutic point of view though their ability to react to each injection seems unimpaired.

Continued study of the bacterial content of the blood in varying intervals after the injection only rarely demonstrates the disappearance of microorganisms present there before the injection. This fact further complicates the already difficult explanation of the action of vaccines.

If a curative effect could be obtained only with a specific



vaccine one would be justified to think of the formation of specific antibodies, though the interval between injection and critical drop of temperature really is too short to make this interpretation fully acceptable. This explanation, however, is unacceptable because all the various vaccines yield the identical effect. Even the inference that we are dealing with an anaphylactic phenomenon cannot be admitted, because this could follow only the injection of a specific vaccine.

As long as the identical reaction as well is observed after the parenteral injection of any of a large number of different protein substances, it probably is safest to interpret the immediate sequelae of vaccine injection simply as a foreign-protein reaction, which produces symptoms similar to, but not identical with, the symptoms of anaphylaxis.

A considerable part of the effect, therefore, can readily be ascribed to the quickened formation of larger quantities of certainly not specific antibodies as the result of the intense stimulation of all cell activity in the body. No particular curative value, however, can be assigned directly to the excessive rise of temperature. From our experience we are convinced that the largest share of credit for the resulting benefit must be given to the never-failing marked hyperleucocytosis.

Only a few words may be added concerning the preparation of such vaccines.

Kraus and Mazza used bacterial cultures, killed with ether; Gilmore preferred to grow the microorganisms for eighteen hours on a sterile blood coagulum, to wash them off and kill them by heating for one hour at a temperature of between 56° and 60° C., finally adding a 0.4 per cent solution of tricresol. Weaver routinely injected streptococci, killed in a 25 per cent solution of galactose, emphasizing that heating but not galactose will destroy the anti-

genic power of the germs. Others killed the bacteria with carbolic acid.

We employed as a rule vaccines prepared in the Serum Institute of Vienna, with bacteria killed both by heat and carbolic acid. As already mentioned, our streptococcic vaccine represented a mixture of various strains all obtained from puerperal sepsis cases, thus it was polyvalent, while the majority of other investigators employ a vaccine prepared only from one strain. Some authors sensitize the vaccine by the addition of the patient's blood serum (Champtaloup) or with an immune serum (Hamm), and claim better results for this so-called simultaneous method. We had no personal experience with the latter.

In the past few years we treated a series of cases with Much's omnadin (Kalle & Co.). It contains a mixture of reactive proteins, a lipid mixture obtained from gall, and a mixture of animal fats. The use of omnadin alone yielded uniformly bad results. The injection of this vaccine usually failed to cause any reaction so that we were forced to the conclusion that this agent certainly would cause an antibody stimulation entirely insufficient for the requirements of a curative effect on a puerperal infection.

I shall illustrate vaccine results on a few case histories. We begin with four cases treated with a specific vaccine.

C. J. forty years old. Admitted Mar. 17, 1914, discharged Mar. 25, 1915.

*History.*—On Mar. 7, spontaneous delivery. Fever on fifth day postpartum, temperature rising to 40° C., chill.

*Stat. pres.*—Subinvolution, feculent fluor. Temperature 40.1° C. Blood culture: streptococci, nonhemolytic.

In next few days lytic fall of temperature to 37.8° C.

Mar. 20. Temperature again up to 40.8° C. Blood culture: streptococci. Intravenous injection of streptococcus vaccine (60 million bacteria). Temperature remains high without change, no reactive chill.

Mar. 21. Another injection of vaccine, same dosis. Same lack of reaction.

Mar. 23. Icterus. No positive local findings. Third injection of same dosage.

Mar. 25. 1915. With gradually diminishing cardiac action, exitus.

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B. A., forty-one years old. Admitted Nov. 17, 1914, died Nov. 22, 1914.

*History.*—Last menses on July first. On day of admission, forenoon, spontaneous expulsion of fetus. Placenta retained. Severe hemorrhage. For this reason sent to hospital.

*Stat. pres.*—Marked anemia. Profuse vaginal hemorrhage.

Incomplete abortion of five months. Digital removal of retained placenta. Saline infusion.

Nov. 18. Fever. Blood culture: streptococci, nonhemolytic.

Nov. 19 and 20. Streptococcus vaccine intravenously, containing 40 million bacteria each). Injections borne without discomfort. No reactive chill.

Nov. 21. Pneumonic infiltration in right lower lobe. Patient became delirious.

Nov. 22, 1914. Pneumonia extended to left side. Patient died later in the evening.

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C. J., forty years old. Admitted Mar. 17, 1914, discharged cured May 22, 1914. (Fig. 24.)

*History.*—Last menstrual flow end of January, less than usually. For past fourteen days fever, chills and hemorrhage.

*Stat. pres.*—Temperature 38° C. Incomplete abortion in third month. Curettage.

Up to Mar. 23, temperature normal.

From this day on for some time continuously high fever, repeated chills. Local findings negative. Some moist râles in lungs. Systolic murmur over apex of heart.

Temperature remains high, but for a few days no chills.

Near end of April again frequent chills. Blood cultures persistently sterile.

Since symptomatic treatment has yielded no result, in spite of negative blood findings, vaccine treatment is taken under consideration. Unexpectedly a new blood culture shows strongly hemolytic streptococci. Therefore, injection of streptococcus vaccine seems fully justified.

May 3. Intravenously, 20 million streptococci. Reactive chill.

May 4. Patient afebrile.

May 5. Intravenous injection of 40 million streptococci. Reactive chill.

May 6. Temperature normal.

May 7. Only slight rise in temperature.

May 8. Intravenous injection of 60 million streptococci. No reactive chill this time.

Blood culture, which remained positive for streptococci after first two injections, after third injection is sterile.

Temperature from then on persistently below  $37^{\circ}$  C.

May 22, 1914. Patient discharged cured.

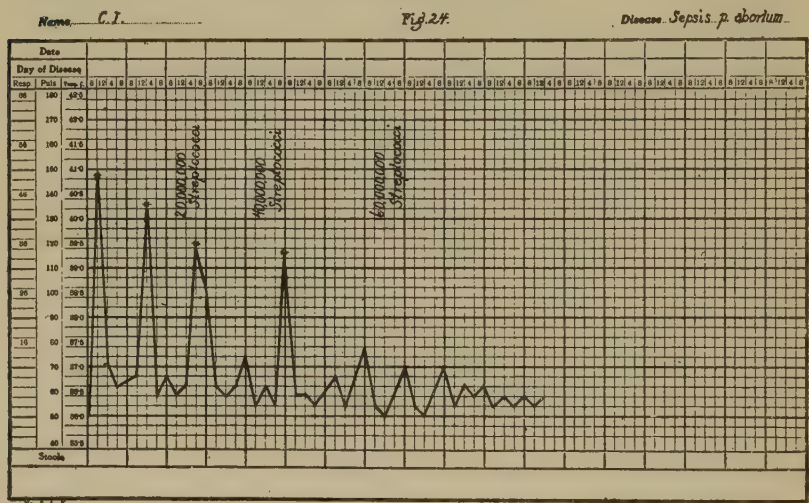


Fig. 24.—Intravenous administration of streptococcus vaccine. After first two injections typical reaction. Chill and critical drop of temperature to normal.

In this instance the beneficial effect of the vaccine is unmistakable. Still the argument might be raised that the patient could have recovered as well without vaccino-therapy.

F. A., forty-two years old. Admitted May 31, 1916, discharged cured Aug. 12, 1916.

*History.*—Placenta previa, version, extraction, removal of placenta.

On third day post partum rise of temperature to  $39.8^{\circ}$  C., chill.

*Stat. pres.*—Negative local findings. Blood culture: *Bacterium coli*, pure culture.

An abscess forms on mons veneris starting from a varicose vein. Incision made.



Phlebitis of right thigh.

Continuously high fever. Several chills. Another blood culture: bacterium coli.

June 24 and 26. Coli vaccine intravenously (60 million bacteria). Reactive chills after each injection.

Several periphlebitic abscesses are opened. Pus contains bacterium coli.

Gradual fall of temperature to normal, with only occasional unaccountable rise to 39° C.

After several weeks of slow convalescence patient discharged well on Aug. 12, 1916.

This case seemed particularly suitable for vaccinothrapy. The injections, however, yielded no effect. Recovery undoubtedly would have occurred also without this therapy. Typical protracted course of a coli infection.

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B. A., thirty-six years old. Admitted Dec. 1, 1915, died Dec. 7, 1915.

*History.*—Last menses early in September. For past week hemorrhage and fever.

*Stat. pres.*—Abortion in third month. Profuse hemorrhage. Temperature 40° C. Curettage.

Dec. 2. Chill. Foul discharge. Blood culture: streptococci. Turpentine injection on left thigh.

Dec. 4. Around point of injection an infiltration, about two cm. in diameter. No fluctuating abscess.

Dec. 5. No abscess. Blood culture: strongly hemolytic streptococci. Intravenous injection of coli vaccine (60 millions). No reactive chill. Some dyspnea.

Dec. 6. Same amount of vaccine given.

Dec. 7, 1915. Meningeal symptoms. Patient is soporous. Exitus.

Case seemed suitable for fixation abscess therapy, but in accord with the experience of French authors the unfavorable outlook was evidenced by the absence of a reactive chill.

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K. A., twenty years old. Admitted Feb. 13, 1918, discharged well Mar. 8, 1918. (Fig. 25).

*History.*—On Feb. 7, spontaneous delivery. Since Feb. 11, high fever and pain in abdomen.

*Stat. pres.*—Small perineal laceration. Starting from it a dirty ulcer running over to right large labium. Uterus poorly involuted. Fundus at level of navel. Adnexa free. Temperature  $39.5^{\circ}\text{C}$ .

Feb. 14. Blood culture: streptococci. First intravenous injection of coli vaccine (40 million bacteria). Three quarters of an hour later chill.

Feb. 15. Afebrile in the morning. Later in day temperature rising to  $39.5^{\circ}\text{C}$ .

Feb. 17. Blood culture: streptococci. Second injection of coli vaccine (80 million bacteria). After 30 minutes reactive chill.

Feb. 18. Highest temperature  $38.3^{\circ}\text{C}$ .

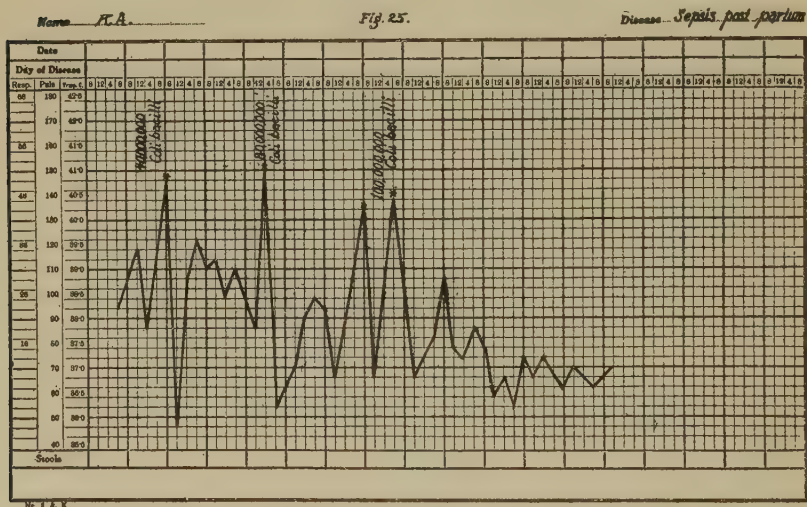


Fig. 25.—Intravenous injections of coli vaccine. Typical reaction with chill and critical drop of temperature.

Feb. 19. Temperature up to  $40.2^{\circ}\text{C}$ .

Feb. 20. Third injection of coli vaccine (100 millions bacteria). Thirty minutes later reactive chill.

During next two days rise to  $38.8^{\circ}\text{C}$ ., from then on temperature remained normal.

Mar. 8, 1918. Discharged cured.

In this case the effect of the administration of vaccine seems self-evident though it does not manifest itself until after the third injection. In spite of our skepticism, we are willing to admit that in this case the curative effect of

the therapy cannot be denied. However, even this case does not represent a perfect illustration of the curative effect of vaccinothrapy, in which the critical drop of the fever should be followed by persistently normal temperature. The case shows well the prognostically favorable reactive chill after each injection.

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J. A., Admitted July 25, 1918, discharged cured Sept. 14, 1918.

*History.*—On July 19 spontaneous delivery. Ever since, fever.

*Stat. pres.*—Infected episiotomy wound, partially closed by sutures. Purulent discharge. Uterus subinvolved. Fundus four fingers above symphysis. Temperatures between 38.8° and 39.2° C.

Blood culture: streptococci in pure culture.

July 29. Typhoid vaccine (100 million bacteria) intravenously. Injection borne well, about 15 minutes later severe chill lasting half an hour.

July 30. No critical fall of temperature, which remains high.

Aug. 2. Vaccine injection (150 million bacteria). Severe chill and on next day critical drop of temperature. Rise in evening.

Aug. 5. Intravenously typhoid vaccine (200 million bacteria). Again reactive chill and critical drop of temperature on the next day, with rise in evening.

Fever continues high.

The injections raise number of leucocytes from approximately 7000 to hardly 8000.

Since there was no apparent effect from vaccinothrapy, it was discontinued. Process became localized with formation of a left parametric infiltration.

After very slow convalescence patient discharged cured on Sept. 14, 1918.

It would be unjustified in this case to ascribe the recovery to the vaccine injections. The patient had good reactive chills but no other influence either on general condition or temperature could be noticed. The outcome undoubtedly would have been the same also without vaccinothrapy.

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M. M., twenty-five years old. Admitted Apr. 7, 1918, discharged cured Apr. 29, 1918.

*History.*—On Apr. 3, delivered spontaneously. Since morning of day of admission fever and chills.

*Stat. pres.*—No physical findings to account for fever. Genital hemorrhage. Uterine fundus three fingers below navel. Adnexa and both parametria free.

Blood culture: sterile.

Apr. 9. Intravenously typhoid vaccine (300 million bacteria). Severe and long reactive chill.

During next few days the former high temperature hardly ever went above 37° C.

Apr. 15. New rise of temperature to 39.2° C. Therefore another vaccine injection (500 million bacteria). Again severe reaction.

Apr. 16. Morning temperature normal, evening up to 39.2° C.

Within next few days temperature fell in steps to normal, which was reached on Apr. 19 and continued to Apr. 29, 1918 when patient was discharged as cured.

Though one cannot assign to vaccinothrapy the rôle of the determining factor in the recovery of this patient, the beneficial effect of each injection cannot be doubted. After the first injection there was a critical drop of temperature, after the second, a lytic fall which lasted.

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H. M., twenty years old. Admitted Mar. 5, 1918, died Mar. 13, 1918.

*History.*—Last menses end of January. For last three weeks uterine hemorrhage.

*Stat. pres.*—Inevitable abortion in third month.

Mar. 7. Spontaneous passage of fetus. On account of hemorrhage digital removal of placenta. Temperature 40.2° C.

Mar. 9. Temperature remains at same level. Blood culture: streptococci. Intravenous injection of gonococcus vaccine (50 million bacteria). No reactive chill.

In next few days no change in temperature or general condition.

Two more vaccine injections are made, again without any result.

Mar. 13, 1918. Patient became delirious and died.

A total failure of vaccinothrapy.

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H. P., seventeen years old. Admitted Oct. 5, 1921, died Nov. 6, 1921 (Fig. 26).

*History.*—Last menses on July 26. For past week hemorrhages. Three days ago fetus expelled, since then fever.



*Stat. pres.*—Uterus somewhat enlarged, soft. External os closed. Left adnexa and parametrium normal. To the right of uterus a round oblong infiltration running to lateral pelvic wall (thrombophlebitis).

Patient's temperature was persistently high, reaching 41° C., with several chills. At first, several doses of mirion were given hypodermically (5 to 10 c.c.), once also intravenously. No effect. Next, 7 doses of tryptaflavin were administered, again failing entirely to change the course of the disease. Finally, a trial was made with Much's omnadin. Same failure.

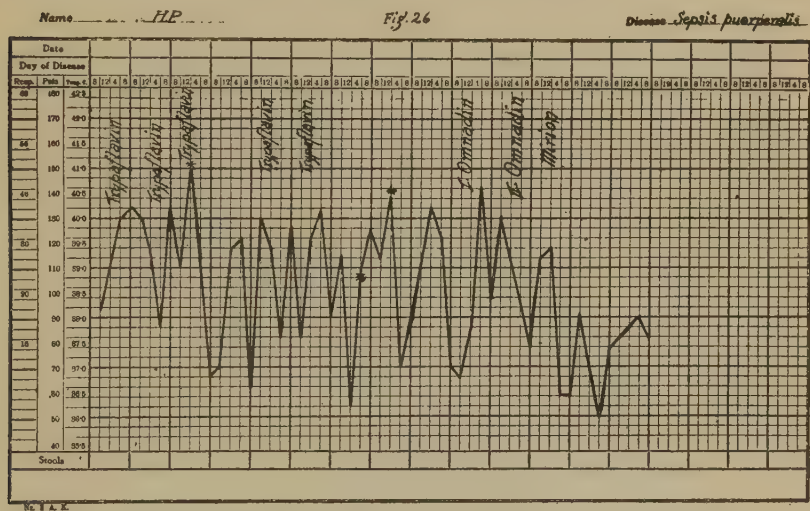


Fig. 26.—Combined treatment with mirion, tryptaflavin and omnadin without any effect.

Patient succumbs, after development of a thrombotic process on the left side and of several pulmonary abscesses, on Nov. 6, 1921.

This case looked hopeless from the beginning, since the bacterial content of the thrombi obviously seemed out of reach for any of the administered antiseptics.

Summarizing our own experience we can say that treatment with vaccines, and especially with heterovaccines, certainly cannot be regarded a panacea; that its results, however, are such that they bear well a comparison with

any other method of treatment so far suggested. It seems possible that their value might be enhanced by certain mixtures of vaccines so that further investigations with them should not be discouraged. Possibly it will be found necessary to inject thousands of millions of bacteria which, when injected intramuscularly, could act as a sort of reserve deposit. In truly desperate cases one might consider the problem of immunization by means of live bacteria, however, I cannot help doubting that very much could be achieved in this manner. It is the characteristic feature just of the puerperal infections that new masses of bacteria are continually thrown into circulation, in particular out of the thrombi. Also these new invasions, like the injections of dead bacteria, are often followed by a critical drop of temperature after an immediate chill, but we certainly have no reason to look upon these repeated chills of repeated "autovaccination" as factors aiding in the recovery of the patient.

**Foreign Proteins (Milk, Aolan,<sup>1</sup> Caseosan<sup>2</sup>).**—It is impossible to enter here in detail into the problem of non-specific protein therapy and I must refer the interested reader to the extensive literature of the past few years, very comprehensively presented e.g., in Petersen's noteworthy book "Protein Therapy and Nonspecific Resistance" (MacMillan Co.).

R. Schmidt, who in 1916 published his results with milk injections must be regarded as the originator of the protein therapy. Stimulated by this report the method in the meantime has been introduced practically into every special field of medicine and as well has been applied in the treatment of puerperal fever.

We had sometime ago attempted to influence the course of puerperal infections by means of injections of milk. Later we resumed investigations along this line but again

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<sup>1</sup>Milk, which is free of bacteria and toxins.

<sup>2</sup>A 5 per cent sterile solution of casein.

have entirely discarded the method. There were several reasons that induced us to take this final step.

First of all we never felt able to explain to our satisfaction what the essential remedial principle in these milk injections is which could account for the effect. It could not be the casein alone, as claimed by some authors, since milk contains many other agents which must participate in the total effect. Next the question of dosage seemed one of great difficulty to us because the chemical constitution of milk, and especially of the milk marketed in a large city, is extremely variable. Not even the milk of the same species of animal can be accepted as a definite chemical mixture because its condition is dependent upon very many changeable factors such as age, nutrition of animal, duration of lactation, to say nothing of almost unavoidable impurities or deliberate adulteration. Therefore even identical quantities of milk by no means represent identical quantities of therapeutically effective constituents. Every sample of milk contains large numbers of microorganisms, of toxins, ptomaines, etc., which are not eliminated by the process of sterilization, but beyond any doubt to a more or less marked degree enter into the clinical picture of the reaction caused by the injection.

Before milk could be accepted as a medicinal agent two questions should be answered definitely. The first and most important is: Which of its constituents is the essential curative factor? Second: In what manner can bacteria and toxins in the milk be reduced or eliminated so that we might exclude incidental symptoms caused only by them after injection?

It seemed for a while that the first point was cleared up by the investigations of Lindig. After several years of careful study he had found that there exists a certain relation between caseolytic action and the amount of protective substances against infection present in the body, and he

had furthermore discovered that the latter can be augmented by the parenteral introduction of casein. In view of the practically identical therapeutic results of injections of either milk or pure casein, he felt justified in deducing that the casein represents the curative element in the whole milk. This conclusion seemed convincing. A most noteworthy addition would thus have been made to therapeutic medicine if Lindig's observations under further tests would have proved correct.

E. F. Mueller, in 1919, however, demonstrated that also other constituents of milk exhibit similar, though weaker, effects; that indeed identical therapeutic results are obtained with milk from which all casein had been removed. It is this latter fact which practically annihilated Lindig's claim. We remain in the same ignorance concerning the active principle in the whole milk.

More progress has lately been made in furnishing an acceptable answer to the second question. E. F. Mueller succeeded in preparing a germ- and toxin-free milk, aolan. It is emphasized by him that this preparation has the great advantage of duplicating the curative effects of milk without the latter's disagreeable immediate sequelae, so that "no energy is wasted in the fight against the milk toxins, and all the reactively produced organ energization is available for curative effect on the infection." Also any danger of an anaphylactic reaction is eliminated. Very recently the Vienna Veterinary School has been furnishing a new milk preparation free of bacteria and toxins, in which this condition of purity is obtained not by a chemical process as in aolan, but by special precautionary measures at the time of milking (Seidel and Hoegler).

I see a further disadvantage of milk therapy in its inaptitude for intravenous administration. Though views are contradictory in regard to the therapeutic value of the immediate reaction—some writers actually object to the



severe general symptoms caused by injections (Schittenhelm, Zimmer)—I personally am of the opinion that the stronger reaction after the intravenous injection of a remedy leads to a more forceful stimulation of those organic processes which provide the protective antibodies; that therefore, on principle, intravenous medication always is preferable to intramuscular injection. However, as far as the puerperal infection is concerned, promptness and intensity of reaction probably play only a rôle of minor importance.

Our own results with the various milk preparations could hardly be called satisfactory.

It was our rule to inject, deeply into the muscles of the gluteal region, 5, 10 up to 20 c.c. of milk, sterilized in a water-bath immediately before use. The gluteal region offers the advantage that in comparison with any other part of the body these injections are less painful and less likely to cause abscesses. The reaction usually was severe, appearing quickly in form of a chill followed by a rise of temperature up to 40° C. or above. For several hours or even days the patient felt weak and tired. Desire to sleep or improvement in patient's sleep, claimed by some observers as a gratifying result of the therapy, we never noticed, occasionally rather the opposite. In some instances the temperature actually fell critically after profuse perspiration, but, as a rule, it soon had returned to its former height. Actual cure by milk injections alone we did not observe in a single case. For this reason and on account of theoretical consideration to which I have referred, we discontinued this form of treatment a few years ago.

Renewing our investigations later with aolan our results were not much better. The reaction it causes certainly is less intense than after milk, even in our later cases when we increased the injected amounts of aolan to 50 and up to 150 c.c. in place of the former maximum of 15 c.c. But even

such doses did not permanently influence favorably the course of the infection. As a matter of fact in many cases they did not cause the critical drop of temperature to normal which occurs relatively often after the injection of whole milk. All this led us to the conclusion that seemingly the patient responds on the whole less well to these special toxin-free preparations than to milk itself.

L. Th., thirty-eight years old. Admitted June 27, 1922, died Sept. 19, 1922 (Fig. 27).

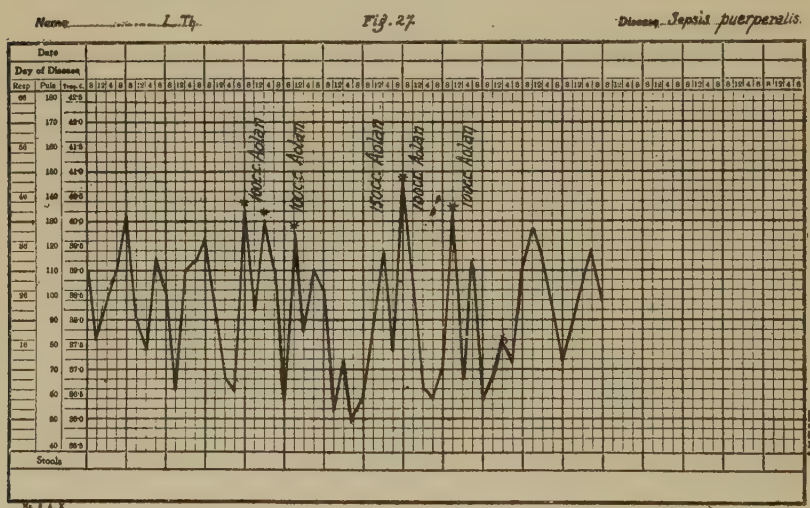


Fig. 27.—Very large doses of aolan (100 to 150 c.c.) without any effect.

*History.*—Spontaneous premature delivery in seventh month, on June 24. Immediately afterwards fever and chill. Ever since high fever up to, and occasionally above  $41^{\circ}$  C.

*Stat. pres.*—Uterine fundus two fingers below navel. Cervical canal open. No palpatory anomalies within pelvis.

Patient since admission has daily chills, therefore

July 3. First intramuscular injection of 100 c.c. of aolan.

July 5. Condition absolutely unchanged. Second injection, same dosis.

July 12, 15, and 17. Aolan, 100 c.c. each time. Effect nil.

Between July 20 and Aug. 1 (see Fig. 27) five more injections of 100 to 150 c.c. of aolan.

Between Aug. 2 and day of death, six more injections of same dosage, also without any effect.

Patient develops a metastatic pneumonic focus on left side with purulent pleuritis requiring several punctures.

Patient sank gradually and died on Sept. 19, 1922.

In this instance almost excessive doses of aolan (100 to 150 c.c.) failed to yield any effect in spite of the relative benignity of the process evidenced by its slow, long drawn out course.

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In a limited number of cases we have tried caseosan, following in respect to method of administration, dosage and intervals between injections, exactly the instructions of Lindig. Extremely intense immediate reactions, which occasionally took an almost alarming aspect after repeated injections, and the fact, that the curative results of caseosan in no way are better than those of any other of the milk preparations finally induced us to discontinue the use not only of this substance but also of its more recently advocated combinations, yatren-caseosan, staphylococcus—and streptococcus-caseosan.

It seems appropriate to refer in this connection to good results recently claimed by Gow with a peptone treatment. A paste is made by mixing 10 gm. of peptone (Witte) with hot distilled water, gradually added to a total quantity of 50 c.c. After the addition of a small amount of sodium carbonate the mixture is boiled, filtered, and the filtrate kept in a hot water-bath for 20 minutes. The initial dose intravenously injected is 8 to 10 c.c. It is given every other day with an increase of each dose by 2 c.c., the final maximal dose being 20 c.c. He finds that in combination with standard or autovaccines the peptone treatment yields eminently satisfactory results, especially by furthering localization of the infectious process.

We likewise experimented with a combination of col-largol or argochrome with caseosan, or serum, vaccine, etc.,

and injected first the protein with the idea that the energization of the body cells resulting from it would enhance the curative value of the secondarily administered antiseptic. Our results with the tested combinations of collargol and milk, argochrome and vaccine, collargol and vaccine were far from encouraging.

M. L., thirty-eight years old. Admitted Apr. 17, 1917, died Apr. 25, 1917.

*History.*—Last menstruation three months ago. Claims she has been flowing for several weeks.

*Stat. pres.*—Temperature 40.2° C. Inevitable abortion in third month.

After expulsion of fetus placenta is extracted.

Apr. 19. Temperature continuously high. Nothing abnormal within pelvis.

Blood culture: Pure streptococci.

For the purpose of sensitizing patient gonococcus vaccine (50 million bacteria) is injected intravenously. No reactive chill, no visible effect on general condition.

Apr. 20. Intravenous injection of 0.2 gm. of argochrome.

Injection is borne well. Temperature remains unchanged.

Apr. 22. A second intravenous injection of argochrome (0.2 gm.), again without any effect.

Apr. 25, 1917. Patient succumbed to severe septic process.

This history is cited simply to illustrate the type of case which led us to arrive at our present pessimistic view concerning the value of a combination therapy.

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F. M., thirty-nine years old. Admitted Mar. 2, 1918, died Mar. 15, 1918.

*History.*—On Feb. 25, spontaneously delivered. Since Mar. 2, fever and chills.

*Stat. pres.*—Temperature 38.2° C., pulse 102. Genital bleeding. Through patent cervical canal soft tissue and blood coagula palpable. Fundus midway between umbilicus and symphysis.

Mar. 3. Temperature remains high. Blood culture: pure streptococci.

Intravenous injection of typhoid vaccine (300 million bacteria). No reactive chill.

Mar. 4. Temperature unchanged. One chill. Otherwise no



change in general condition. Blood culture still positive for streptococci.

Mar. 5. Typhoid vaccine intravenously (500 million bacteria). Very soon after injection patient had a chill, but no other effect.

Mar. 7. Third typhoid vaccine injection (500 million bacteria). No effect outside of reactive chill.

Since the vaccine alone apparently was not benefiting patient, in the next few days two intravenous injections of argochrome, 0.2 gm. each, were given. They also failed to change the course of the infection and the patient died on Mar. 15, 1918.

Even repeated injections of vaccine were unable to sensitize the patient sufficiently to render the argochrome, given later, more effective.

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One should not be surprised at the failure of such a combination therapy to yield better results, since as a matter of fact the active curative factor of each of the agents probably is the same. Whether we employ milk, any of the milk preparations, vaccine, serum or colloid metals, all we can expect from them is the effect either of leucostimulation or of the introduction of a foreign protein, therefore the combination of various substances essentially can result in nothing else but a mere summation of single effects. A multiplied therapeutic effect, as so well shown by Buergi, can be anticipated from a combination of medicinal agents only if each of them has a specific action of its own. This is not the case with the constituents of the combinations so far advocated and tried in the treatment of puerperal sepsis.

### Serotherapy

Encouraged by the results that have been obtained with sera, especially in the treatment of diphtheria, the obstetrician naturally approached with exalted hopes the problem of serotherapy of puerperal infections. I might state at the outset, he met with great disappointment. Very little is left of the original enthusiasm and but rarely an

obstetrician today depends on injections of serum in the treatment of a septic puerpera.

Again I shall refrain from a detailed discussion of the nature of sera, their preparation, of complements or amboceptors, but refer those interested to modern textbooks. It suffices to state that against the streptococcic infections, in which we are chiefly interested, sera of certain animals, rarely of man, have been employed chiefly on the supposition that they exert a directly antibacterial effect. However, their curative value has also been explained on other grounds.

Bohnstedt, e.g., thinks that the serum of Gabritschewsky in particular affects the membrane covering the coccus, so that the alexins and complements of the blood are permitted to pass through it and kill the germ. Through its disintegration endotoxins and proteins are set free which have to be neutralized in the blood. If the latter contains complements in sufficient quantity to obtain this required neutralization, then it is possible that all the microorganisms will be destroyed.

Meyer prepared a serum for which he claims not only bactericidal but as well antitoxic powers. He infected animals with a pure culture of a streptococcic strain highly pathogenic for the animal. Another series of animals was next treated with a mixture of the obtained specific antibacterial serum and this strain of streptococcus, it being assumed that the added streptococci are dissolved in the serum and thus specific endotoxins liberated. In this manner Meyer thought to have endowed his serum with antitoxic qualities. This claim, however, was repudiated by Aronson, who demonstrated that quite unlike the typhoid or cholera bacillus, the streptococcus cannot be dissolved by body fluids, but is rendered innocuous solely by leucocytes. For this reason the endotoxins of a streptococcus, as can be shown in experiments, cannot be liberated in the

manner suggested by Meyer. If it is impossible that a mixture of serum and streptococci could contain free endotoxins, the injection of such a mixture cannot produce antitoxins.

All practical experience supports Aronson's contention, and extensive experimentation has proved that filtrates of streptococcus cultures contain no, or only minimal amounts of, toxin; that serum fails to cause bacteriolysis of streptococci, and that therefore in this manner antitoxin formation certainly cannot be stimulated.

The sera on the market in general are polyvalent animal sera procured by immunization with various strains. Some of them include in their preparation, passage through animals (Marmorek), others do not require this step (Menzer, Meyer-Ruppel, Paltauf, Tavel, or Roux), while Aronson's serum, as pointed out, embodies both modes.

Particular efficacy is claimed by Krongold-Vinaver for a serum described in 1921. It is obtained by infection of horses with a human streptococcus, highly virulent for mice. Eighty c.c. of a 24 hour ascites-bouillon culture are injected into a horse and the serum procured by a venesection which is made 14 or 15 days later. A prophylactic injection of 0.1 c.c. of this serum into a mouse 24 hours before infection protected the animal against a dosis of streptococci representing 100 times the lethal dose. In treating cases of puerperal sepsis this author injected intravenously on the first day 20 c.c. of the serum with 180 c.c. of saline solution, on the second day 30 c.c. of serum with 270 c.c. of saline, and on the third day 40 c.c. of serum with 360 c.c. of saline. He reports to have cured 38 patients out of a total of 41 who showed streptococci in the cervix, and two out of five who had streptococci in the blood.

Hunton produced a polyvalent serum by injecting horses with 8 different strains of streptococci. This serum apparently is still extensively used by American physicians.

It was originally prepared from 35 cultures of streptococci, which, however, later were found to represent only eight different species.

In view of the undeniable existence of many essentially different species of streptococci, it is not surprising that no marked specific effect can be expected even from the so-called polyvalent serum. It is more than doubtful that the employed serum actually, if at all, will contain a sufficient amount of the specific antistreptococcic substance required in the individual case.

A truly specific effect could be anticipated only from an autoserum, but if we remember the obstacles presenting themselves in actual practice even in the preparation only of an autovaccine, we must realize the futility of any hope in this respect. The manufacture of a serum requires a great deal more time. A streptococcic infection probably would have passed through its entire course before the specific autoserum would be at hand.

No more practical seems the suggestion of Heimann, i. e., to use on a patient only that serum which has proved effective on a mouse infected with the streptococcus responsible for the patient's infection. In a case of this sort, time is too valuable to wait for the development of the artificial infection in the animal, and to test on it then various sera to ascertain which one exhibits a curative effect. Moreover, as I have repeatedly pointed out in foregoing chapters, since the mode and spread of a puerperal infection is so essentially different from that in the artificially infected animal, curative results obtained on the latter do not necessarily indicate what could be expected from the application of this same serum to a septic puerperal woman.

Likewise the claim, that human sera, e.g., the sera of convalescent patients (Zangemeister, Meissl) yield particularly good results, must be looked upon with suspicion. They could prove truly valuable only if obtained from patients



recovered from an infection with the identical strain of streptococcus. A possible advantage of human sera lies in the fact that they, better than animal sera, might supply to the sick patient certain complements which in her blood are present only in deficient amounts. Zangemeister considers this difference in the complement content as the actual cause of therapeutic failures with horse serum and thinks that the difference in the streptococcic strains really is of no significance.

The experiments of Zangemeister and Meissl are based on observations of Ehrlich, in 1898, which tended to show that for the production of therapeutic sera it is more advantageous to use animals which biologically stand nearer to man than the horse. Apes furnish complements decidedly more closely related to those of the human being.

For obvious reasons under present conditions the wholesale preparation of ape sera is practically impossible, but at least theoretically this proposition looks plausible. However, other investigations of Aronson demonstrated conclusively that there exists no necessity for the employment of closely related or of homologous sera. In experimenting on infected monkeys with various sera, he discovered that horse serum afforded exactly as much prophylactic protection as monkey serum.

If the difference in effect were actually dependent solely on the complement contents, then any polyvalent horse serum could be rendered effective by the mere addition of some human blood serum. There should not be seen any therapeutic failures with them, and the convalescent serum certainly should have yielded decidedly better results than it actually has done.

We find no encouragement in the use of these convalescent sera from the experiments of Heynemann. In infected mice, he found that the serum of a normal healthy puerpera seemingly retarded the process, while serum of a puerpera,

recovering from a streptococcic sepsis, indeed did not delay but often hastened the animal's death. In not a single instance did this latter serum exhibit any curative effect.

The trials of Meissl on puerperal septic patients with convalescent serum likewise failed to prove any advantage. Of 16 patients treated in this manner only six recovered and in most of them the infection was strictly limited to the uterus. Very few had positive blood-culture findings. This percentage of cures is not remarkable. It has been obtained with other modes of therapy and certainly does not establish any special efficacy of convalescent serum. Also Bartram reported from the clinic in Tuebingen recoveries only in a limited number of cases treated with the sera of normal pregnant women or of patients recovering of a sepsis, with normal human serum and with the serum of the patients themselves. Freund fails to recognize any superiority of convalescent serum and thinks that the main cause of the inefficiency of all streptococcus sera lies in the fact that streptococci by passage through an animal so quickly change their virulency that it is impossible to produce a serum whose antibodies would prove specific for streptococci pathogenic for man.

There is still another argument that can be raised against any theoretical assumption of a noteworthy advantage of convalescent sera.

An actual accumulation of specific antibodies could be expected in a patient only immediately after the successful finish of her fight against the streptococcic infection. This debilitated and weakened individual is hardly a fit subject from whom to withdraw a sufficient quantity of blood. Therefore of necessity the venesection is performed only a long time after a patient has recovered from a sepsis. This, however, is almost senseless in view of the well-known fact that a streptococcic infection (erysipelas, puerperal infection) procures for the patient no long lasting immu-

nity and no protection against the repetition of the same infection.

I shall mention one more reason why one might hesitate to make use of convalescent sera.

I had the opportunity to observe some of Meissl's patients with him. I know the individuals from whom he obtained the serum for the treatment of other patients. One woman, on recovering from her puerperal sepsis, later developed a cervical carcinoma which required a radical operation. Though there was a long interval between these two diseases, it would be impossible to assert that at the time of venesection she did not shelter in her body those still unknown factors causing the development of carcinoma. Certain recent findings of characteristic blood changes in cancer patients (serologic carcinoma diagnosis), in the light of our utter ignorance concerning the actual mechanism of cancer transmission, at least suggest the possibility, however remote, of cancer transference in this manner. A preliminary serologic study on the donor will not be of much value because the reaction is found negative also in some patients evidently affected with a carcinoma, while again it has been found that a certain percentage of sera of pregnant and puerperal women give a positive blood serum reaction for carcinoma. Pregnancy is seemingly prone to impair the reliability of certain serum tests (tuberculosis, syphilis) and for this reason extreme caution is required in the employment of this particular convalescent serum.

Delmas recommends direct transfusion of human blood instead of serum injection. It is supposed to stimulate the bone marrow and leucocyto-genesis and also to directly transfer antibacterial and antitoxic substances. Large blood transfusions (up to 1000 c.c.) are extensively employed by American obstetricians who enthusiastically advocate them as decidedly superior to serum injections

(Hirst, Broadhead, Thalhimer and Hogen). Others again prefer the repeated injections of only small quantities of blood (Piper, Polak). All my objections to human serum apply as well to blood transfusion.

Equally questionable appears the suggestion of Leith-Murray to inject antistreptococcic serum together with normal horse serum. The streptococcus serum being bacteriolytic, it requires complements from the patient. Since she is unable to supply them in sufficient quantities, he thinks the efficacy of the remedial serum is improved by the addition of complements. Since human complements are less able than horse complements to activate the latter, he injects, as mentioned, also normal horse serum. In opposition I might refer once more to the finding of Zangemeister that the complements of horse serum fail to exert this effect in the human body. From all these facts one can but draw the conclusion that the antistreptococcus horse serum by itself can have only very little therapeutic value since not even the addition of either horse or human complements, as has been suggested, lead to its further activation.

According to Bailey, however, serum which has been impaired in its physiologic activity by being kept for some time in an ice box, can be reactivated by the addition of fresh human serum (1:160) or the serum of guinea pigs (1:10). Nevertheless, all available information forces us to the deduction that a specific effect of these therapeutic sera is extremely doubtful.

It might even be doubted that a specific effect would be of any advantage. A bacteriolytic action, e.g., might indeed prove disastrous through inundation of the system with the toxic products of extensive bacterial disintegration. At the start of an infection when the circulation of bacteria in the blood stream still is limited, the amount of available antibodies is only just sufficient to take care of them. From this viewpoint it seems obvious that serum



treatment could exert a truly valuable effect only in the incipient stage of the infection. The correct gauging of the curative effect of a remedy which must be employed very early, "immediately after the first rise in temperature," is practically impossible in the face of the fact that the clinical course of puerperal infections can never be foreseen, and in view of the common experience that in large numbers they terminate favorably without any therapeutic effort. Only a combined antibacterial-antitoxic serum (Meyer) could hold out any hope but, as shown above, the preparation of such a serum is impossible.

Against any necessity of employing a specific serum speaks the satisfactory experience of French writers with the Petit serum, a horse serum which on three consecutive days had been heated to 56° C.

We observed in a few instances a pleasing effect with streptococcus serum although the infections were caused by other bacteria, e.g., *Staphylococcus aureus* or *bacterium coli*.

Eichhorst wrote on the successful treatment of a staphylococcus septicemia with antistreptococcus serum, while Schapiro and Impassato recorded one case each of cure of a puerperal infection with diphtheria serum.

Therefore, I do not consider valid any longer the former demand that streptococcus serum should be employed only if streptococci are recovered either from the blood or the lochia.

Likewise the investigations of Kolle, Sachs and Georgi tend to prove in a certain sense the lack of specificity in sera. These writers discovered that normal serum as well affords a certain amount of protection against a gas bacillus infection and that also a nonspecific factor enters in its curative effect. However, the same amount of prophylactic and remedial effect could be obtained only by using much larger doses of normal serum than of specific serum.

These experiments not necessarily have any bearing on the problem of the efficacy of sera chiefly characterized by their antitoxic ability, as, e.g., tetanus or diphtheria serum, but it is claimed by Bingel that in 466 cases of diphtheria he obtained with simple horse serum the identical results as in 471 other cases treated with the antitoxic diphtheria serum.

Though antistreptococcic sera have no specific effect, we admit that they occasionally exert a beneficial influence which we then must ascribe to some other factor contained in them.

Our own experience seems to support the view of Aronson, Petit and Bergey, and others, that the useful serum effect, especially in the case of a streptococcic infection, in the main is due to its influence on the leucocytes, causing either an increase of their number or an intensified avidity with which they attack the microorganisms. In his answer to Zangemeister, Aronson some time ago emphasized that serum by itself is not bactericidal but for the purpose of destruction of germs is dependent upon help from the leucocytal apparatus, a fact particularly true as far as the destruction of streptococci is concerned. If leucocyto-genesis is defective, sera are void of any curative effect.

Petit considers normal horse serum, which he used, the best activator for the formation of polynuclear leucocytes, while according to Murtry it stimulates phagocytosis. Bergey furnished strong support to these contentions by experiments. He found that *in vitro* the addition of serum alone did not retard the growth of streptococci but that this was accomplished by the further addition of leucocytes, and then as the result of phagocytosis. He came to the conclusion that the body battles against a streptococcic infection not so much with antitoxins and alexins as by means of phagocytosis.

The existing relations between serum effect and leuco-

cytes have been elucidated by the investigations of Neufeld and Rimpau. They found that antistreptococcus serum is neither antitoxic nor directly bactericidal, but that it neutralizes an immune body within the bacterium, rendering the latter less resistant to the phagocytic power of the white cells. Very similar is the opinion of Menzer. Also American writers (e.g., Bailey) emphasize this relation of serum to the leucocytic apparatus and consider the rise of the opsonic index and the increase of immune opsonins respectively, subsequent to serum injection, as facts of great importance.

In the cases in which we used serum, we observed constantly a marked hyperleucocytosis, but only of short duration, as is the case whenever it is produced by artificial stimulation. An additional factor of significance in the curative effect is the general energization which is achieved by serum as with any other injected protein substance.

With serum action established as nonspecific, there really exists no justification for advocating the therapeutic use of antistreptococcus or any other serum in the treatment of puerperal infections since it is relatively expensive and not entirely free of all risk. Useful are only very large doses which in most cases have to be repeated more than once. With increasing and repeated doses the patient is exposed to the possibility if not probability of various disagreeable consequences, such as pain in joints, serum exanthema, etc., even of anaphylactic shock if a new injection is required some time after the preceding.

Loetsch, in our opinion, is wrong in looking upon serum exanthema as a welcome sign that the fight against the infection is won. Some sensitive patients, as is well known, develop this exanthema after only a prophylactic injection of serum, that is, when there actually is no infection existing.

We can easily dispense with serum because we possess

other remedies with which we can provoke a hyperleucocytosis and a nonspecific effect, with decidedly less discomfort to the patient.

If this is all we can expect from the employment of serum we must not be disappointed in its very restricted curative value. As several times before emphasized by me, it is an almost characteristic feature of a puerperal infection, especially in its hematogenic form, that its main foci, the thrombi, are actually cut off from the circulating blood and therefore, the microorganisms lying well sheltered in them, are shielded against any phagocytic action of even a largely increased number of leucocytes. To employ serum with any hope of gratifying effect one would have to make every injection just before a new bacterial invasion is about to occur so that a new army of leucocytic warriors would stand ready to give prompt battle to the new horde of invaders. A therapy whose success then is almost entirely dependent upon mere intuition or good luck, obviously can never prove a really useful method.

In our skeptical opinion concerning serum therapy we do not stand alone. It is fully shared by Haase, Hagemann, Mayer, Rubeska, Stowe, etc., while others, like Schauenstein, more cautiously state that serotherapy is "not necessarily effective,"—but is employed by them because "it is harmless."

We find that American writers likewise have expressed themselves unfavorably in regard to the therapeutic value of sera, ascribing to them at best only a nonspecific effect. Hannah could not see any better results from antistreptococcic serum than from normal horse serum. Fisher concluded that one could observe seemingly good effect about as often as no effect at all, and that it is a fact that very many of the cases get well without any therapy. Also Broadhead emphasized that the results with or without serum are approximately the same. Baldwin regarded sero-



therapy as absolutely valueless, while Erck ventured the opinion that whiskey proves about as efficacious as serum.

Thus we notice exactly the same divergence of opinions also among American gynecologists, since at least some of them, especially in recent years, again advocate the use of a polyvalent streptococcus serum. Lately a change can be observed in regard to the dosage which more generally, it seems, has been increased from the original 10 to 20 c.c. to 50 to 200 c.c. and even more. As a rule now on the first three days, intravenously, 150 c.c. each are given and, if required, smaller quantities subsequently. The total quantity averages 450 to 600 c.c. though not so rarely in some cases up to 900 c.c. are used (Hirst, Williams). One of the most ardent defenders of serotherapy is Bailey who, as already mentioned, explains its efficacy on the basis of an increase of immune opsonins. The serum is active only as long as it can be re-activated by the addition of complements (human or animal). Bailey is more cautious than others in regard to dosage and repeats the injections only if the temperature remains high. In view of the likelihood of severe reaction with a sharp rise of temperature, he recommends to inject serum only at the moment when the fluctuating temperature has reached its lower level. A high temperature without any remissions, therefore, in his opinion contraindicates serum. To reduce all the possible risks of the therapy to a minimum, he demands that patients, who are likely to require larger quantities, be tested for a possible hypersensitiveness against serum. Such patients usually will develop a reactive erythema after the injection of only 2 c.c. Patients reacting positively to this test can be desensitized by repeated injections of minimal quantities of serum, beginning with one drop and gradually increasing to one c.c.

For obvious reasons we have tried antistreptococcic serum only in a few of our cases, and with expectations

not high, our disappointment naturally was not great; but we considered it our duty to test also this remedy as one more link in the long chain of similar remedies advocated in the therapy of puerperal infections.

I might repeat in this connection from preceding chapters that some authors believe they derived special benefit from a combination of antistreptococcic serum with other substances or methods, e.g., with fixation abscess (Funk-Brentano, Roulland), with collargol, vaccination (Girling, Ball, Murray, Bailey), methylene blue or argochrome (Schaefer).

Since the only possible curative factor in each of the two components of such a combination probably is the same, though possibly different in the degree of action, the combination can result only in a summation of effects but never can yield a specific or particularly favorable result. It required but a few exact clinical observations to convince us of the correctness of our theoretical considerations and to induce us to discontinue any further tests on patients.

Deserving further attention is only the procedure of Levy and Hamm. They employed, both prophylactically and therapeutically, a vaccine in which the bacteria had been killed with phenol, and which they had sensitized with immune serum. All the prophylactically treated women had an afebrile puerperium with the exception of one who died of a coli peritonitis. The peritoneal exudate in this case showed no streptococci although a hemolytic type had been previously discovered in the vaginal secretions. In another series the injections were made every other day for curative purposes. Of four cases with positive blood findings two recovered, of four with negative blood findings all recovered.

When discussing the problem of prophylaxis in general I had occasion to mention the various arguments against the value of protective vaccination which has been advocated

e.g., by Joetten and Louros. I can add here only that statistics based on so small a number of cases, permit of no conclusive deductions, in regard to puerperal morbidity or mortality, because innumerable other factors actually determine the course of the puerperium. The absence of streptococci in the peritoneal exudate of the case of Levy and Hamm, just quoted, does not positively prove that the prophylactic injections had an immunizing effect against the hemolytic streptococci previously found in the vaginal secretions. It is possible that a few streptococci within the peritoneal cavity had merely been outgrown by the many coli bacilli. Moreover it is a well-known fact that hemolytic streptococci in the vagina of a pregnant woman by no means always cause an infection of the peritoneum with the same organism. Positive blood findings are not incompatible with final recovery of the patient, and therefore, a 50 per cent cure in four cases with positive blood cultures is neither startling nor an infallible proof of the efficacy of the remedy employed.

If in one of our patients no decided improvement could be seen after one or two serum injections, she was always offered the possible benefit of some other type of treatment. So a combination of serum with other modes of therapy was also employed by us, not simultaneously but successively. As guide in the treatment, outside of temperature, pulse and general condition, we use chiefly the behavior of the leucocytes. A marked hyperleucocytosis is always accepted as a favorable sign of good effect and encourages us to continue with the same method of treatment. However, serum injections as a rule increased but slightly the number of white cells.

I wish to emphasize, that this leucocytic reaction, especially in the negative sense, is not necessarily the ominous sign of certain failure. I well remember several cases in which the leucocytes did not increase, indeed some in which the count fell, and who nevertheless finally recov-

ered. As in so many other respects also here we see how thoroughly unaccountable is the course of a puerperal infection; how uncertain the outlook in the individual instance; how difficult to evaluate the rôle played by therapy in the recovery of a patient.

In this connection I may mention that we have made use of serum, not necessarily of streptococcic serum but for economic reasons chiefly of plain horse serum, for still another purpose. We thought we might obtain by means of subcutaneous or intravenous injection of serum that general energization of body cells we are accustomed to see after parenteral introduction of milk, vaccines or other foreign proteins. It seemed that serum, so easily given intravenously, would have the advantage of a less stormy reaction. If we did get a reactive chill, we hoped that the sensitized body might respond better to the effect of other agents, as e.g., collargol. The results were not marked enough to encourage us to continue these tests.

A few words must be said about Deutschmann's yeast serum. First used only by oculists it finally found its way into the therapy of puerperal fever. Literature seems to indicate that it has failed to meet with much popularity. While in ophthalmic practice, on account of the small doses required, the serum was prepared from rabbits, the gynecologists made use of a horse serum, manufactured in the following manner: Horses are fed with increasing doses of yeast. Their serum finally exhibits an extraordinary protective power against infections in animals injected with it.

Since it proved effective against the pneumococcus as well as against strepto- and staphylococcus, it seemingly is polyvalent, but it is neither antitoxic nor antibacterial, and fails to raise either the white count or the opsonic index. It is assumed that as the result of very complex chemical processes, in the end a substance is produced contained



in the serum, which can be transmitted to another animal. This substance is supposed to endow all body cells with renewed strength and energy.

Outside of this rabbit and horse yeast serum, there exists still a serum E of Deutschmann. The addition of cold water causes the precipitation of a substance which is rendered soluble in water by the addition of caustic soda and neutral salts. This E-serum has double strength and thus permits the administration of larger doses with less risk of a serum exanthema. The experiments of Neisser and Guerini showed that the Deutschmann sera increase phagocytosis. We have never employed these sera but the absence of favorable reports in literature presumably indicates that in practice they have failed to fulfill expectations.

In surveying the sum total of results obtained with medicinal treatment of the systemic infection of puerperal fever we find that apparently all the substances, which for this purpose are introduced by the parenteral route, exert approximately the same effect, to be sure, with definite quantitative differences in the obtained reaction. But the degree of reaction is not necessarily proportionate to the degree of curative effect. All of them more or less intensively influence the hematopoietic system, as a rule in the sense of a marked increase of the leucocytes, a phenomenon which only rarely fails to follow injection. Practically all of them presumably possess the ability of stimulating the vital energy of body cells.

In general it seems irrelevant whether we are employing agents of alleged bactericidal power, bichloride, quinine and its combinations, metal colloids, etc., or administer the so-called activators of cellular energy, milk, vaccines, any foreign protein, or make use of substances which are assumed to render innocuous the toxic products of bacterial activity. In the present state of our information we must conclude that we always are actually dealing solely with the effect of protein substances, parenterally introduced. Body

reactions, released in this manner, at times affect favorably the course of the infection. It seems of no particular consequence, however, whether this reaction, looked upon as an energization of cellular activity, is produced by a chemotherapeutic remedy, a concentrated salt solution, a bacterial protein, a vegetable albumin or a colloid substance. Exhaustive investigations of recent date as a matter of fact have shown that not only the various substances just enumerated, but others, like dyes, iodine or turpentine will cause body reactions seemingly identical in every respect.

For this reason certain disputes are entirely out of place. It is of no consequence whether Boettner or Voigt is right in the respective claim that the effect of a colloid is or is not dependent upon the presence of certain protective colloids (*Schutzkolloid*) in them. It cannot be surprising that silver-hydrosols, as emphasized by Voigt, are effective in spite of the absence of a protective colloid. They are by themselves capable of causing cell energization. The addition of a protective colloid might increase this capability, but not necessarily so, because in the administration of a mixture one of the constituents may conceivably act not in the same sense with all the others, but by a contrary effect, may reduce the total action.

Of course, much is still mere theory, waiting for additional support or actual verification by further investigations and observations. For the present we must be satisfied to assume that identity of resulting reactions justifies the conclusion that there exists at least a close similarity between the agents which produce them.

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In conclusion I will add a small selection of histories of patients who, though seriously sick, recovered without any specific therapy. It seems quite natural that if in any of these cases such a therapy had been employed, the result

very likely would have been credited to the remedy and not to the particular constitutional equipment of this patient or to a low virulency of the bacteria, though the one or the other of these two factors, if not both, actually account for the favorable outcome.

P. A., nineteen years old. Admitted Jan. 31, 1916, discharged cured Mar. 17, 1916.

*History.*—On Jan. 28, delivered spontaneously. Next day fever and chills.

*Stat. pres.*—Sanguinopurulent vaginal discharge. Cervical canal open. Fundus two fingers below navel. Parametria slightly tender to pressure. Temperature 40.1° C. Chill.

Feb. 2. Temperature continuously high (40.2° C.). Rough breath sounds over both lungs. Blood culture: streptococci, slightly hemolytic.

Feb. 9. Continually high temperatures. Several chills. Fine crepitant râles over right lung.

Feb. 16. After having been afebrile and subfebrile for a few days patient's temperature again rose to 40° C.

Feb. 18. Critical fall of temperature which from then on remained normal.

Mar. 7, 1916. Discharged cured.

High fever, many chills and positive blood culture definitely qualify this case as very serious. Treatment was only symptomatic but patient recovered.

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L. M., thirty years old. Admitted June 23, 1916, discharged cured July 15, 1916.

*History.*—Spontaneous delivery on June 21. Since night of 23rd, chills.

*Stat. pres.*—Bloody discharge. Cervical canal gaping. Fundus of uterus midway between umbilicus and symphysis. Temperature 39.8° C.

June 25. Chill. General and local findings negative. Blood culture: streptococci, slightly hemolytic.

June 27. Marked general icterus. Slight dullness to percussion at base of right lung. Temperature remained high.

July 1. For no noticeable reason temperature sank to 37.8° C.

July 2. Temperature normal.

Patient remains afebrile. The unimportant pulmonary symp-

toms disappear quickly and patient is discharged on July 15, 1916.

High temperature, persisting for some time, positive blood culture, and especially the marked general icterus can leave no doubt that this was a severe infection. Patient received only heart stimulants and sedatives, occasionally an antipyretic but recovered.

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G. E., twenty-three years old. Admitted Aug. 12, 1917, discharged cured Aug. 30, 1917.

*History.*—Last menses middle of June. For twenty-four hours severe hemorrhage.

*Stat. pres.*—Patient very anemic, unconscious. Profuse bleeding from vagina. Uterus corresponds to pregnancy of two months, soft. On account of hemorrhage uterus is immediately emptied. Saline infusion. Stimulants.

In the next few days fever up to  $38.8^{\circ}\text{C}$ ., but no chill.

From Aug. 18 to Aug. 24, temperature rising to  $40.3^{\circ}\text{C}$ ., one or more chills daily. Blood culture: pure streptococci.

No other treatment outside of moist packs and occasionally an antipyretic.

Aug. 25. Without visible cause temperature fell to normal.

Temperature remained normal until discharged on Aug. 30, 1917.

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F. J., thirty-three years old. Admitted Aug. 13, 1918, discharged cured Aug. 30, 1918.

*History.*—On Aug. 28, normal partus. Claims to have had chill on fifth day postpartum and eight days later a genital hemorrhage. Ever since, fever.

*Stat. pres.*—Temperature  $38.8^{\circ}\text{C}$ . Patient very anemic. Profuse vaginal hemorrhage. Through gaping cervical canal placental tissue can be felt. Fundus midway between navel and symphysis.

On account of the hemorrhage uterus was emptied at once manually.

Next day hemorrhage stopped. Temperature remained high between  $39.6^{\circ}$  and  $40.1^{\circ}\text{C}$ .

Aug. 16. Along left lateral pelvic wall a tender mass, thickness of finger. Blood culture: streptococci, markedly hemolytic.

The phlebitis in left parametrium extends further and on in-



ner surface of left thigh develops an infiltration, size of palm of hand.

Beginning Aug. 20, gradual fall of temperature.

Aug. 23. Highest temperature  $37.2^{\circ}$  C.

For next few days temperature remained at same level.

Aug. 30, 1918. Patient discharged on her request for further care at home.

In spite of positive blood culture, a phlebitis in paravaginal plexus of veins and a metastasis on the thigh, this patient recovered without any specific therapy. This case could have easily tempted one to perform a ligation of veins.

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D. R., twenty years old. Admitted Mar. 3, 1918, discharged cured Apr. 5, 1918.

*History.*—Delivered spontaneously ten days ago, puerperium undisturbed. On day before admission suddenly fever and a chill.

*Stat. pres.*—Temperature  $38.5^{\circ}$  C., pulse 144. Abdomen somewhat distended and tender to pressure. Vaginal hemorrhage. Uterus subinvolved. Uterine fundus two fingers below navel. Adnexa free.

Blood culture: only staphylococci.

To hasten involution a few injections of ergot are given. Otherwise treatment only symptomatic.

Temperature continues for some time around  $39^{\circ}$  C. Repeated blood cultures remain positive for staphylococcus.

Mar 30. Without evident reason temperature drops to  $36.2^{\circ}$  C.

Temperature remains normal until patient is discharged cured on Apr. 5, 1918.

A severe general infection can be surmised from the repeated positive blood cultures and the continuous high temperature. Under entirely symptomatic treatment patient recovered.

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The undeniable fact, that cases of this sort in considerable number are seen not only by us but by all experienced obstetricians, demands extreme caution in evaluating the

effect of a remedy employed in the treatment of any case of puerperal infection. It would be easy, though neither desirable nor necessary, to quote several other illustrative observations in which patients recovered without any particular therapy in spite of pulmonary or pleuritic metastases, severe icterus, or other complications generally accepted as infallible proof of a serious systemic infection.

The careful analysis of our own experience and a critical study of the records in literature, I confess, fail to yield gratifying or even encouraging final deductions concerning the present status of our ability to cure patients suffering from puerperal infections.

A rational therapy of puerperal fever is seemingly still an unsolved problem. Only a relatively small percentage of these unfortunate women actually recover, and if we are willing to be truthful to ourselves, we must admit our therapy aids but little in the happy outcome.

Convincingly good results cannot be proved for any form of therapy so far suggested and tried. Certainly not much hope can be placed in operative interference. This we were taught both by experience and by studies at autopsies. The future chances of medicinal treatment and especially of chemotherapy seem somewhat better. They at least have not brought entirely negative results. There is reason to hope that along these lines some day the truly etiologic-curative remedy might be discovered. Although the day of its discovery is possibly far distant we must not fear lest it never be reached.

Difficulties must not discourage us, but rather encourage us in the effort to overcome them. Let us remember: Where there is a will, there is a way.

## LITERATURE

### General Papers (Prophylaxis, Systemic Treatment, etc.)

- Abel*: Aerztl. Rundschau, München, 1903, xiii, 138.  
*Alcrudo*: Arch. d. ginecopat., obst., y ped., 1921, xxxiv, No. 9, ref. Jahresb. u. d. ges. Gynäk. u. Geburtsh., 1923.  
*Altmann*: Internat. Jour. Surg., 1904, xvii, 265.  
*Asch*: Verein der Breslauer Frauenärzte, ref. Monatschr. f. Geburtsh. u. Gynäk., xviii, 448.  
*Baisch*: Beihefte zur Med. Klin., 1907, p. 267.  
*Barth*: Deutsch. med. Wehnschr., 1904, Vereinsbeilage, No. 8.  
*Bateman*: Lancet, London, 1905, i.  
*Baumann*: Verein der Breslauer Frauenärzte, ref. Monatschr. f. Geburtsh. u. Gynäk., xviii, 448ff.  
*Benneke*: Pommersche Gesellsch. f. Gynäk., ref. Monatschr. f. Geburtsh. u. Gynäk., xviii, 76ff.  
*Bishop*: Cleveland Med. and Surg. Reporter, 1903, xi, 369, ref. Frommels Jahreshb., 1903.  
*Blair-Bell*: Brit. Med. Jour., 1921, p. 693.  
*Boldt*: Am. Jour. Obst., 1906, liii.  
*Bondy*: Ergebn. d. Chir. u. Orthop., 1913.  
*Bourman*: Clin. Jour., 1921, 1, No. 29, ref. Jahreshb. u. d. ges. Gynäk. u. Geburtsh., 1923.  
*Boyd*: Am. Jour. Obst., 1906, liii.  
*Bricker*: Am. Jour. Surg., 1907, xxi.  
*Brodhead*: Am. Jour. Obst., 1906, liii.  
*Brunner*: Korrespondenzbl. f. Schweizer Aerzte, 1903, xxxiii.  
*Buist*: Lancet, London, 1903, i, 1174.  
*Bumm*: München med. Wehnschr., 1921, No. 46.  
*Burtenshaw*: Med. Record, New York, 1903, lxiv, 677.  
*Byers*: Brit. Gynec. Jour., 1903, xix.  
*Calcagni*: La Rassegna d' obstet. e ginec., 1903, xii, Nos. 10 and 12.  
*Cannaday*: Am. Jour. Obst., 1907, lvi.  
*Carnus*: Thèse de Paris, 1905.  
*Catinal*: Presse méd., 1920.  
*Cerecedo*: Rev. de med. y cirug. práct., 1909, lxxxv, ref. Frommels Jahreshb., 1910.  
*Clifton*: Am. Jour. Obst., 1906, liii, 775.  
*Corner*: Clin. Jour., xxxvi, 151.  
*Coulbourne*: Alabama Med. Jour., 1904, xvi, 435, ref. Frommels Jahreshb., 1904.  
*Cragin*: Am. Gynec. Soc., Am. Gynec., 1903, No. 6; Am. Jour. Obst., 1906, liii, 775.  
*Croke*: Med. Record, New York, 1903, lxiv.  
*Danforth*: Jour. Surg., Gynec. and Obst., 1905, xxvii.  
*Daniel*: Rev. de chir., 1906, ref. Zentralbl. f. Gynäk., 1907, No. 3.  
*Davis*: Am. Gynec. Soc., Am. Gynec., 1903, No. 6; Philadelphia Med. Jour., 1903, xi, 864.  
*Delphoy*: Med. Record, New York, 1903, lxiv.

\*The literature is quoted only beginning with 1903. The enormous number of contributions precludes the possibility of their complete citation. A comprehensive list of papers, published between 1889 and 1903, will be found in Herff's article in Winckel's *Handbuch der Geburtshuelfe*.

- D'Erchia*: Gyn.—Kongress zu Genua, 1908, ref. Frommels Jahresb., 1908.
- Dietrich*: Therap. Halbmonatschr., 1921, xxxv, No. 24.
- Dodd*: Milwaukee Med. Jour., 1905-1906, v, 259, ref. Frommels Jahresb., 1906.
- Doederlein*: Deutsch. med. Wehnschr., 1904, No. 49.
- Doleris*: Ann. de gynéc. et d'obst., 1906, iii, series 2; La Gynec., 1906, xi, 1.
- Donald*: Jour. Obst. and Gynec. Brit. Emp., 1909, xvi.
- Egglessen*: Mississippi Med. Month., October, 1910, ref. Frommels Jahresb., 1910.
- Eschund Schroeder*: Ztschr. f. Geburtsh. u. Gynäk., lxx.
- Fellner*: Berl. klin. Wehnschr., 1909, No. 21.
- Fisher*: Pennsylvania Med. Jour., 1916, p. 399.
- Fraenkel, M.*: Heilkunde, Berlin, 1905.
- Frank*: New York Med. Jour., 1915, p. 726.
- Friedman*: Boston Med. and Surg. Jour., 1921, clxxxv, 617.
- Friedrich*: Pommersche Gesellsch. f. Gynäk., Monatschr. f. Geburtsh. u. Gynäk., xviii.
- Fromme*: Fortschr. d. Med., 1910, Nos. 36 and 37.
- Fry*: Am. Gynec. Soc., Am. Gynec., 1903, No. 6; Am. Jour. Obst., 1907, lvi, 234.
- Galabin*: Practitioner, 1905, lxxiv.
- Georgiini*: Rev. de chir., 196, ref. Zentralbl. f. Gynäk., 1906, No. 45.
- Giliani*: Med. Record, New York, 1903, lxiv.
- Glitsch*: Med. Korrespondenzbl. d. württembergischen ärztl. Standesvereines, Stuttgart, lxxiii, 469, 509.
- Gonzales*: Arch. di ginecopat., obst., y ped., 1921, xxxiv, No. 12, ref. Jahresb. u. d. ges. Gynäk. u. Geburtsh., 1923.
- Gordon*: Practitioner, 1905, lxxiv; Jour. Obst. and Gynec. Brit. Emp., 1907, xi, 17; Lancet, London, 1907, i; Brit. Med. Jour., 1908, i; Jour. Obst. and Gynec. Brit. Emp., 1908, xvi; Lancet, London, 1908, No. 5; Hospital, London, 1910-1911, xlix, 99, ref. Frommels Jahresb., 1910.
- Gradewitz*: Verein d. Breslauer Frauenärzte, ref. Monatschr. f. Geburtsh. u. Gynäk., xviii, 448.
- Haberlin*: Korrespondenzbl. f. Schweizer Aerzte, 1903, No. 33.
- Hager*: Pommersche Gesellsch. f. Gynäk., ref. Monatschr. f. Geburtsh. u. Gynäk., xviii, 76ff.
- Halban*: Zentralbl. f. Gynäk., 1921; Sitzungsber. d. Akad. d. Wissensch., 1896, cv.
- Hamlin*: Jour. Surg., Gynec. and Obst., 1905, xxxii.
- Hammerschlag*: Deutsch. med. Wehnschr., 1905, No. 9.
- Hammerschlag and Magnus*: Deutsch. med. Wehnschr., 1904, Vereinsbeilage, No. 3.
- Harney*: St. Louis Clinique, 1907, xx, ref. Frommels Jahresb., 1907.
- Harrison*: Am. Jour. Obst., January, 1903, p. 104ff.
- Henkel*: Sitzungsber. d. Versammlung deutsch. Naturf. u. Aerzte, Köln, 1908.
- v. Herff*: Korrespondenzbl. f. Schweizer Aerzte, 1903, No. 33; in Winckel's Handb. d. Geburtsh., 1906, iii, Part 2; Sitzungsber. d. intern. med. Kong. zu Budapest, 1909.
- Hirsch*: Med. Klin., 1905, i.
- Holladay*: Am. Jour. Obst. and Gynec., 1923, vi, No. 3.
- Holmes*: Clin. Rev., 1904-1905, xxi, ref. Frommels Jahresb., 1905; New York Med. Jour., 1905, lxxii, 1200.
- Hood*: Massachusetts Med. Jour., 1905, xxv, 193, ref. Frommels Jahresb., 1905.
- Horrocks*: Lancet, London, 1903, ii, 1582; Brit. Med. Jour., 1904, i, 350.
- Hussy*: Monatschr. f. Geburtsh. u. Gynäk., xliii, No. 3.
- Jackson*: Am. Jour. Obst., July, 1906, xiv.
- Jakoby*: Berl. klin. therap. Wehnschr., 1905, p. 442.
- v. Jaschke*: Jahresb. f. ärztl. Fortbild., 1921, No. 7.



- Jeannin*: Jour. d'obst., de gynec. et de ped. prat., 1905, ix, 20.
- Jentzer*: Korrespondenzbl. f. Schweizer Aerzte, 1903, xxxiii.
- Jung*: Med. Klin., 1907, No. 42, p. 1253; Deutsch. med. Wehnschr., 1916, Nos. 13-15.
- Keim*: Les medications nouvelles en obstet., Paris, Bailliere, 1908.
- King*: Internat. Med. Jour., December, 1914, ref. Zentralbl. f. Gynäk., 1915, No. 14.
- v. Klein*: Deutsch. med. Wehnschr., 1904, Vereinsbeilage No. 8.
- Klein*: Strassburger med. Zeitung., 1907, No. 4.
- Knipe*: Tr. New York Obst. Soc., 1916.
- Kreutzer*: Milwaukee Med. Jour., 1905, xiii, 191, ref. Frommels Jahresb., 1905.
- Kroemer*: München med. Wehnschr., 1907, Nos. 1-4.
- Krol*: Berl. klin. Wehnschr., 1913, No. 4.
- Küstner*: Verein d. Breslauer Frauenärzte, ref. Monatschr. f. Geburtsh. u. Gynäk., xviii, 448ff.
- Law*: Denver Med. Times, 1906-1907, xxvi, ref. Frommels Jahresb., 1907.
- Lea*: Brit. Med. Jour., 1905, i.
- Lean*: Am. Jour. Obst., 1906, liii.
- Le Dentu*: Bull. méd., Paris, 1905, xix, 417.
- Lehmann*: Med. Klin., 1906, No. 51.
- Lenhartz*: Nothnagels spez. Path. u. Therap., 1903, iii, Part IV.
- Lewer*: Ztschr. f. ärztl. Fortbild., 1906, iii, 429.
- Läpmann*: Therap. Monatschr., 1908, No. 1.
- Lloyd*: Australia Med. Jour., 1910, xv, 353, ref. Frommels Jahresb., 1910.
- Loebinger*: Verein d. Breslauer Frauenärzte, ref. Monatschr. f. Geburtsh. u. Gynäk., xviii, 448ff.
- London Internat. Med. Congress*, August 6-12, 1913: *Lepage* (Paris): Immediate Curettage also in Presence of Adnexal Affection; *Polak* (Brooklyn): No Curettage in Case of Streptococcic Infection, in Latter Condition (Hemolytic Type) Protective Wall of Infiltration is Missing (?); *Munro Kerr* (Glasgow): Finger Dilatation; *De Lee* (Chicago): Results of His Inquiry by Questionnaires; *Rouland* (Paris): Laparotomy; *Boyd* (Philadelphia): Digital Removal; *Veit* (Halle a. d. S.); *Giffard* (Madras, India): Curettage, Tincture of Iodine; *Nage* (Berlin): Active Therapy; *Hastings* (Dublin): Manual Removal; *Doederlein* (München): Roentgenradiation; *Jakobs* (Brussels): Roentgenradiation.
- Lynds*: Jour. Michigan Med. Soc., 1904, iii, 28, ref. Frommels Jahresb., 1904.
- Magalhaes*: Med. des San Paulo, 1904, vii, 155, ref. Frommels Jahresb., 1904.
- Martin*: Birmingham Med. Rec., 1902, lii, 337.
- Martin*: Pommersche Gesellsch. f. Gynäk., ref. Monatschr. f. Geburtsh. u. Gynäk., xviii, 76.
- Marz*: Med. Rec., New York, 1906, lxix.
- McCann*: Lancet, London, 1905, i; London Adlard. and Son, 1906.
- McIlwraith*: Canada Lancet, 1905, xxxviii, ref. München med. Wehnschr., 1905, No. 33, p. 1601.
- McLean*: Am. Gynec. Soc., Am. Gynec., 1903, No. 6.
- Meek*: Canada Pract. and Rev., 1904, xix, 61, ref. Frommels Jahresb., 1904.
- Metcalf*: Jour. Michigan Med. Soc., 1903, ii, 131, ref. Frommels Jahresb., 1903.
- Montgomery*: Med. Rec., New York, 1903, lxiv, 630.
- Montgomery*: Pennsylvania Med. Jour., 1917, p. 465.
- Moritz*: Pommersche Gesellsch. f. Gynäk., ref. Monatschr. f. Geburtsh. u. Gynäk., xviii, 76.
- Müller*: Dissertation, Marburg, 1903; Korrespondenzbl. f. Schweizer Aerzte, 1903, xxxiii.

- Müllerheim*: Deutsch. med. Wehnschr., 1904, Nos. 6 and 7.  
*Murray*: Am. Gynec. Soc., Am. Gynec., 1903, No. 6; Am. Jour. Obst., 1906, liii.  
*Natanson*: Thèse de Paris, 1908.  
*Noble*: Am. Jour. Obst., 1907, lvi, 189.  
*Norris*: Am. Med., 1904, vii, 256.  
*Oldfield*: Brit. Med. Jour., April, 1910, i, 872.  
*Opitz*: Deutsch. med. Wehnschr., 1904, Nos. 25 and 26; in Menge-Opitz, Lehib. d. Frauenheilk., 1920.  
*Panecky*: Deutsch. med. Wehnschr., 1905, No. 9.  
*Pasek*: Arch. f. Gynäk., 1912, xviii, 8.  
*Peiser*: Verein d. Breslauer Frauenärzte, ref. Monatschr. f. Gebrutsh. u. Gynäk., xviii, 448.  
*Peri and Balard*: Rev. franc. de gynéc. et de obst., 1921.  
*Piet and Perrin*: Jour. de sc. méd. de Lille, 1904, i, 545.  
*Petruschky*: Deutsch. med. Wehnschr., 1905, No. 9.  
*Pichevin*: Semaine gynéc., 1907, 249.  
*Pinard*: Rev. prat. d'obst. et de paediat., 1903, xvi, 14.  
*Pinkham*: Am. Jour. Obst., 1913, lxi, 113.  
*Polak, J.*: Tr. Am. Gynec. Soc.; Am. Jour. Obst., lii, 100; Jour. Am. Med. Assn., May 6, 1910.  
*Pribram*: Zentralbl. f. Chir., 1919, No. 48.  
*Pryor*: Am. Jour. Obst., January, 1903, p. 104ff.  
*Queissner*: Deutsch. med. Wehnschr., 1905, No. 9; Monatschr. f. Geburtsh. u. Gynäk., xix, 38.  
*Quinones*: Arch. de gynec., 1910, xxiii, 261, ref. Frommels Jahresb., 1910.  
*Radtger*: Deutsch. med. Wehnschr., 1905, No. 9, p. 366.  
*Randon*: Am. Jour. Obst., 1906, liii.  
*Recasens*: Rev. de med. y cirug. práct., 1904, lii, 161, ref. Frommels Jahresb., 1904.  
*Resinelle*: Sitzungsab. Gyn.-Kongress zu Genua, 1908, ref. Frommels Jahresb., 1908.  
*Rosenstein*: Verein der Breslauer Frauenärzte, ref. Monatschr. f. Geburtsh. u. Gynäk., xviii, 393.  
*Rosinski*: Deutsch. med. Wehnschr., 1904, Vereinsbeilage No. 8.  
*v. Rosthorn*: Deutsch. med. Wehnschr., 1905, No. 23.  
*Rouet*: Rev. gén. de clin. et de therap., 1906, xxii; Jour. de Prat., 1906, ix, 15.  
*Runge*: Berl. klin. Wehnschr., 1908, No. 11.  
*Sachs*: Frauenärzte, 1909, xxiv, 530.  
*Sahli*: Korrespondenzbl. f. Schweizer Aerzte, 1903, xxxiii.  
*Schütze*: Deutsch. med. Wehnschr., 1905, No. 9.  
*Semon*: Deutsch. med. Wehnschr., 1904, Vereinsbeilage, No. 8.  
*Sikes*: Internat. Therap., 1905, i, 227.  
*Simon*: Thèse de Paris, 1909.  
*Sinclair*: Surg., Gynec. and Obst., November, 1907.  
*Stangenberg*: Deutsch. med. Wehnschr., 1904, Vereinsbeilage, No. 8.  
*Stark*: Practitioner, 1921, cvii, No. 4.  
*Stone*: Philadelphia Med. Jour., June, 1903; Am. Jour. Obst., 1903, p. 104; New York Med. Jour., 1903, lxxvii, 1165.  
*Taft*: Yale Med. Jour., 1904, xi, 41, ref. Frommels Jahresb., 1904.  
*Tucker*: Am. Jour. Obst., 1906, liii.  
*Turenne*: Ann. de gynéc. et d'obst., August, 1907.  
*Veit*: Prakt. Ergebn. d. Geburtsh. u. Gynäk., 1909.  
*Vineberg*: Am. Gynec. Soc., Am. Gynec., 1903, No. 6, p. 550.  
*Walhardt*: Sitzungsab. d. Gyn.-Kongress zu Strassburg, 1909; Zentralbl. f. Gynäk., 1909; in Stoeckels' Lehrb. d. Geburtsh., 1920.  
*Watkins*: Illinois Med. Jour., 1903, v, 21; Chicago Med. Recorder, 1903, xxiv, 212; Am. Jour. Obst., 1909, lx.

- Watson*: Clin. Med. Rec., September 15, 1903.  
*Wernitz*: Volkmanns Sammlung klin. Vortr. N. F., No. 352.  
*v. Werth*: Korrespondenzbl. f. Schweizer Aerzte, 1903, xxxiii.  
*Wetherill*: Am. Jour. Obst., 1903, xlvii, 590.  
*Williams*: Am. Gynec. Soc., Am. Gynec., 1903, No. 6.  
*Wilson*: Lancet, London, 1909, ii.  
*Winter*: Deutsch. med. Wchnschr., 1905, No. 9; Sitzungsab. d. Gyn.-Kongress zu Strassburg, 1909; Zentralbl. f. Gynäk., 1909.  
*Wormser*: Sitzungsab. d. Gyn.-Kongress zu Strassburg, 1909, Zentralbl. f. Gynäk., 1909.  
*Wylie*: Am. Jour. Obst., January, 1903, p. 104ff.  
*Zangemeister*: Prakt. Ergebn. d. Geburtsh. u. Gynäk., 1909, i.

### Uterine Lavage, etc.

- Adam*: Intercolonial Med. Jour. Australasia, 1904, ix, 277, ref. Frommels Jahreshb., 1904.  
*Allison*: Med. Age, 1904, No. 20, ref. Frommels Jahreshb., 1904.  
*Arias*: Rev. de med. y cirug. práct., 1904, No. 823; ref. Zentralbl. f. Gynäk., 1904, No. 45, p. 1373.  
*Arndt*: Dissertation, München, 1912, ref. Zentralbl. f. Gynäk., 1913, p. 1310.  
*Batini*: Boll. d. Soc. tosc. di ostet. e ginec., 1903, ii, No. 6, p. 152, Firenze.  
*Berthod*: Gaz. d. mal. infant., 1905, vi.  
*Boissard*: Bull. Soc. d'obst. de Paris, September 1, 1906, p. 141.  
*Boissard and Condert*: Bull. Soc. d'Obst. de Paris, 19, xi, 3; L'Obst. étique, 1904, No. 1, p. 75; Jour. des Pract., 1904, iii, 5.  
*Bouchacourt*: Bull. Soc. d'Obst. de Paris, September 1, 1906.  
*Boyd*: Ann. Gynec., June, 1904.  
*Brindeau*: Bull. Soc. d'Obst. de Paris, September 1, 1906.  
*Brinkley*: Virginia Med. Semi-Month., 1915, p. 10.  
*Buman*: Rev. méd. de la Suisse romande, 1905, 20, x, p. 641-684.  
*Cabanes*: Gyn.-Kongress, Algier. Rev. Pratique de Gynec. d'Obst. et de Med., September 15, 1907; Ann. de Gynec., 1907, No. 2; Bull. méd. de l'Algérie, 1904, xv; Med. Press and Circular, 1904, lxxviii, 38.  
*Champetier des Ribes*: Bull. méd., Paris, 1905, xix, No. 49.  
*Chandler*: Obstetrical Society Philadelphia, 1904, iv, 7; New York and Philadelphia Med. Jour., 1904, No. 23, p. 1088; Louisville Month. Jour. Med. and Surg., September, 1904. Discussion, Ann. Gynec., June, 1904, p. 339.  
*Charles*: Jour. d'accouch., Liège, 1907, xxviii.  
*Chavanne*: Poitiers, Méd. Poitiers, 1903, xvii, 22, 40.  
*Clement*: Thèse de Paris, 1907.  
*Coudrain*: Thèse de Paris, 1904.  
*Davidson*: Illinois Med. Jour., 1903, v, 266.  
*Demelius*: Bull. Soc. d'Obst. de Paris, September 1, 1906, p. 141.  
*D'Erchia*: La Ginecologia, Rivista pratica, Firenze, 1904, Fasc. 6, p. 176.  
*Doederlein*: Strassburger Gyn.-Kongress, 1909.  
*Dowd*: New York Med. Jour., 1915, p. 221.  
*Dufous-Lammartine*: Thèse de Paris, 1906.  
*Ethier*: Rev. méd. du Canada, 1903, vii, 253, 263.  
*Fonteilles*: Thèse de Paris, 1904.  
*Fournier*: Bull. Soc. d'Obst. de Paris, September 1, 1906.  
*Fowler*: Chicago Med. Recorder, 1903, xxiv, 395.  
*Frederiqu*: Bull. Soc. belge de gynéc. et d'obst., 1905-1906, xvi.  
*Füth*: Zentralbl. f. Gynäk., 1906, No. 35.  
*Furtin*: Thèse de Paris, 1904.  
*Gallant*: New York Med. Jour., 1906, lxxxix, 261.  
*Gonzalo*: Rev. de med. y cirug., 1907, lxxv, ref. Frommels Jahreshb., 1907.  
*Gordon*: Lancet, London, 1905, i, 1095.

- Grandin*: Med. Rec., New York, 1903, lxiv, 157.  
*Guenniot*: Bull. Soc. d'Obst. de Paris, September 1, 1906.  
*Hammon*: Thèse de Paris, 1907.  
*Hirst*: Ann. Gynec., June, 1904.  
*Hubbard*: Am. Jour. Obst., 1906, xiv.  
*Ill*: Am. Jour. Obst., April, 1911.  
*Keller*: Sitzungsber. d. Strassburger Gyn.-Kongress, 1909.  
*Lepage and Pozzi*: Compt. rend. Soc. de obst. et de gynec. et de paed. de Paris, July, 1905.  
*Norris*: Ann. Gynec., June, 1904.  
*Pasturand*: Thèse de Paris, 1905.  
*Patek*: Arch. f. Gynäk., xcvi.  
*Paucot*: Nord. méd., Lille, 1905, xi, 104; Bull. et mém. Soc. méd.-chir. du nord, Lille, 1905, i, 46.  
*Pedraja and Tanago*: El siglio med., 1908, xl, ref. Frommels Jahreshb., 1908.  
*Perrenot*: Thèse de Lyon, 1904.  
*Philipp*: München med. Wehnschr., 1921, No. 38.  
*Pichevin*: Semaine gynéc., 1906, No. 7; Jour. d'accouch., Liège, 1905, x, 8; Bull. Soc. d'Obst. de Paris, 1905, No. 8, p. 209; Semaine gynéc., 1905, x.  
*Picqué*: Bull. Soc. d'Obst. de Paris, 1905, No. 8, p. 209.  
*Pinard*: Rev. prat. d'obst. et de paediat., 1905, xviii, 165-173; Bull. méd., Paris, 1905, xix, No. 49; Rev. de gynec., 1905, ix, No. 5, p. 912.  
*Plympton*: Gaz. de gynéc., 1903, Nos. 1-4.  
*Raich*: Jour. akuscherstwe i shenskich bollest. (russ.), May and June, 1907, ref. Frommels Jahreshb., 1907.  
*Raphael*: Therap. Monatsh., September, 1906, xx.  
*Rasis*: Thèse de Paris, 1906.  
*Riss*: Gyn.-Kongress, Algier, Rev. prat. de gynéc., d'obst. et de pédiat., September 15, 1907; ann. de gynec., 1907, No. 2.  
*Risso*: Arch. de gynec., Barcelona, 1906, xix, 107.  
*Rossi*: La Rassegna d'Obstet. e gynec., 1905, xxvii, No. 1, p. 36.  
*Sabadini*: Gyn.-Kongress Algier, Rev. prat. de gynec., d'obst. et de pédiat., September 15, 1907; Ann. de gynec., 1907, No. 2.  
*Safford*: Med. Rec., New York, 1923, p. 536.  
*Schechner*: Berl. klin.-therap. Wehnschr., 1905, p. 252.  
*Schlüter*: Dissertation, Strassburg, 1910.  
*Schweitzer*: Monographie, 1913; Zentralbl. f. Gynäk., 1914, No. 9.  
*Sitsinsky*: Monatschr. f. Geburtsh. u. Gynäk., xx, p. 641.  
*Soubejran*: Gaz. d. hôp., 1907, No. 36.  
*Tissier*: Bull. Soc. d'Obst. de Paris, September 1, 1906.  
*Toff*: München med. Wehnschr., 1904, No. 49; Sitzungsber. d. Versammlg. deutsch. Naturf. u. Aerzte, 1904, ref. Zentralbl. f. Gynäk., 1904, No. 43.  
*Traugott*: Ztschr. f. Geburtsh. u. Gynäk., 1911, lxviii, No. 2; Zentralbl. f. Gynäk., 1913, No. 52.  
*Vignes*: Gynec. et obst., 1920, ii, No. 3, ref. Zentralbl. f. Gynäk., 1921, No. 28, p. 1027.  
*Wallich*: Bull. méd., Paris, 1905, xix, No. 49.  
*Waltherdt*: Zentralbl. f. Gynäk., 1911, No. 2.  
*Walther*: Med. Klin., 1905, No. 3.  
*Watson*: Brit. Med. Jour., 1923, i, 505.  
*Weil*: New York Med. Jour., 1909, lxxxix.  
*Weiss*: Rev. med. Cubana, April, 1904, ref. Jour. méd. de Bruxells, 1904, No. 47, p. 647.  
*Wetherill*: Am. Med., 1904, vii, 189.  
*Wiggin*: Internat. Clin., 1904, iv, 221.  
*Wilson*: Ann. Gynec., June, 1904.  
*Wilson*: Med. Jour., South Africa, 1922, p. 112, rev. in Am. Jour. Obst. and Gynec., 1923, vi, No. 4.



- Winter*: Zentralbl. f. Gynäk., 1906, No. 18; Zentralbl. f. Gynäk., 1908, No. 46; Strassburger Gyn.-Kongress, 1909; Zentralbl. f. Gynäk., 1910, No. 48; Zentralbl. f. Gynäk., 1911, No. 15, p. 43; Med. Klin., 1911, No. 16.
- Witchouse*: Brit. Med. Jour., 1920, ii, 267.
- Zweifel*: Deutsch. med. Wehnschr., 1904, No. 17; Monatschr. f. Geburtsh. u. Gynäk., xxxix, No. 4; Arch. f. Gynäk., 1908, lxxxvi, No. 6; Zentralbl. f. Gynäk., 1913, N<sup>o</sup> 39; Med. Klin., 1914, p. 1428.

### Hysterectomy

- Albertin and Jambon*: Lyon méd., 1906, No. 16.
- Asch*: Verein der Breslauer Frauenärzte, 1903; Monatschr. f. Geburtsh. u. Gynäk., xviii.
- Bacon*: Jour. Am. Med. Assn., 1903, xl, 1049.
- Bergesit*: Gior. di ginec. e di pediat., 1903, xiii, No. 13, p. 197.
- Berritti*: Gior. di ginec. e di pediat., 1905, No. 4.
- Boldt*: Am. Jour. Obst., 1904, 1, 99; *ibid.*, xlvi, 295; Tr. New York Obstetrical Society, 1905, iv, 11; Am. Jour. Obst., 1905, lii; New York Med. Month., 1905, xvii, 367.
- Bovin*: Ztschr. f. Prof. J. Berg, Nordisk med. Ark., 1911, xlv, ref. Frommels Jahreshb., 1911.
- Brauham*: Am. Assn. Obst. and Gynec., September 19-21, 1905; Am. Jour. Obst., 1905, lvii, 717.
- Brothers*: Med. Record, New York, 1907, lxxi.
- Cabanes and Vicent*: Bull. méd. de l'Algerie, 1904, xv, 78, ref. Frommels Jahreshb., 1904.
- Carstens*: Am. Assn. Obst. and Gynec., September 19-21, 1905; Am. Jour. Obst., 1905, lvii, 717.
- Catinal*: Presse méd., 1920, No. 4.
- Cestan*: Toulouse méd., 1903, v, 188, ref. Frommels Jahreshb., 1903.
- Cocque*: Gaz. de gynéc., 1903, Nos. 1-4.
- Cooke Hirst*: Am. Jour. Obst., June, 1912.
- Cortejarena*: 14 Congress internat. de méd. à Madrid. L'Obstetrique, 1903, p. 347; Siglo med., Madrid, 1904, li, 51, ref. Frommels Jahreshb., 1904.
- Cortiguera*: 14 Congress internat. de méd. à Madrid, 1903, L'Obstetrique, 1903, p. 347.
- Cotte*: Gynec. et obst., 1921, iv, No. 3, ref. Zentralbl. f. Gynäk., 1922, No. 42, p. 1027.
- Cristeanu*: Rev. de chir., 1904, Nos. 8-10, ref. Frommels Jahreshb., 1904; Rev. de gynéc. et de chir. abd., 1904, viii, 617.
- Cumston*: Am. Assn. Obst. and Gynec., September 19-21, 1905; Am. Jour. Obst., 1905, lvii, 717; Tr. Am. Assn. Obst. and Gynec., 1906, xviii.
- Dam*: Clinique, Bruxelles, 1904, xviii, 261, ref. Frommels Jahreshb., 1904.
- Daniel and Eicou*: Arch. gén. de méd., 1905, i, 597-615.
- Deaver*: New York Med. Jour., 1904, lxxix, 10; Am. Jour. Obst., April, 1904, p. 504.
- Deletréz*: Jour. de chir. et ann. Soc. belge de chir., 1903, iii, 121, ref. Frommels Jahreshb., 1903; Ann. de l'Inst. chir. de Bruxelles, 1903, x, 84, ref. Frommels Jahreshb., 1903; Congress nat. périod. de gynéc., d'obst. et de paediat., 1904, ref. Frommels Jahreshb., 1904; 19 Congress franç. de chir., Semaine méd., 1906, p. 471.
- Doleris*: Ann. de gynéc. et d'obst., 1903, lix, 379; La Gynécologie, 1903, viii, 105; *ibid.*, 1904, ix, 97; Scalpel, 1921, lxxiv, No. 17, ref. Jahreshb. ueber d. ges. Gynäk. u. Geburtsh., 1923.
- Donnet*: Limousin méd., Limoges, 1905, xxix, ref. Frommels Jahreshb., 1905.
- Druebert*: Écho méd. du nord, Lille, 1905, ix, 523, ref. Frommels Jahreshb., 1905.
- Duret*: Jour. d. sc. méd. de Lille, 1903, i, 313, ref. Frommels Jahreshb., 1903; Semaine gynéc., 1903, viii, 49.

- Faure*: La Gynécologie, November, 1909.
- Feis*: Therap. d. Gegenw., 1903, No. 5, p. 220.
- Fergusson*: Edinburgh Med. Jour., 1906, xix; Jour. Obst. and Gynec., Brit. Emp., 1906, ix, No. 5.
- Gallant*: Am. Assn. Obst. and Gynec., September 19-21, 1905; Am. Jour. Obst., 1905, lvii, 717; Thèse de Paris, 1905.
- Gordon*: Brit. Med. Jour., 1909, i.
- Goullioud*: Lyon méd., ciii, 91.
- v. Herff*: Deutsch. med. Wchnschr., 1908, Nos. 24-26.
- Hermosa*: Gac. méd., Mexico, 1903, iii, 298, ref. Frommels Jahresb., 1903.
- Jewett*: Am. Gynec., 1903, ii, 118.
- Kiriak*: Gaz. de gynéc., Paris, 1903, xviii, 172.
- Koblanck*: Ztschr. f. Geburtsh. u. Gynäk., lxiv, No. 3.
- Krönig*: Strassburger Gyn.-Kongress, 1909.
- Küstner*: Verein der Breslauer Frauenärzte, 1903; Monatschr. f. Geburtsh. u. Gynäk., xviii.
- Kufferath*: Bull. Soc. belge de gynéc. et d'obst., Bruxelles, 1903-1904, xiv, 49; Presse méd. belge, 1903, lv, 793, ref. Frommels Jahresb., 1903.
- Labhardt*: Zentralbl. f. Gynäk., 1909, No. 23.
- Lapointe*: Clinique, 1906, i.
- Latzko*: Wien. klin. Wchnschr., 1907, No. 19, p. 553.
- Lea*: Jour. Obst. and Gynec., Brit. Emp., 1903, No. 2, p. 132.
- Lemoine*: Jour. méd. de Bruxelles, 1904, ix, 543, ref. Frommels Jahresb., 1904; Jour. de chir. et ann. Soc. belge de chir., 1904, iv, 193, ref. Frommels Jahresb., 1904.
- Lop*: Gaz. d. hôp., 1906, lxxix, 284.
- Mauclair*: Semaine gynéc., 1903, viii, 257, 265.
- Maurique*: Rev. med. de Boydta, 1905-1906, ref. Frommels Jahresb., 1906.
- Miles-Porter*: Am. Assn. Obst. and Gynec., September 19-21, 1905; Am. Jour. Obst., 1905, lvii, 717.
- Mouchotte*: Ann. de gynéc. et d'obst., 1904, series 2, i, 164; Thèse de Paris, 1903.
- Pankow*: Ztschr. f. Geburtsh. u. Gynäk., lxvi, No. 2, p. 213.
- Peri and Ballard*: Rev. franc. de gynéc. et d'obst., July, 1921, ref. Zentralbl. f. Gynäk., 1921, No. 42, p. 1710.
- Pfannenstiel*: Mittelrhein. Ges. f. Geburtsh. u. Gynäk., 1903, ref. Monatschr. f. Geburtsh. u. Gynäk., xvii, 69.
- Pichevin*: Semaine gynéc., 1903, ix, No. 17; *ibid.*, 1904, ix, 13.
- Pinard*: 14 Congress Internat. de méd. à Madrid, 1903; Ann. de gynéc. et d'obst., April, 1903, p. 241; Internat. Clin., 1904, iv, 234, ref. Frommels Jahresb., 1904.
- Potvin*: Gynec. et obst., 1921, iv, No. 3, ref. Zentralbl. f. Gynäk., 1921, No. 42, p. 1709.
- Schickele*: Beitr. z. Geburtsh. u. Gynäk., xvi, No. 1.
- Schüller*: Verein der Breslauer Frauenärzte, 1903, ref. Monatschr. f. Geburtsh. u. Gynäk., xviii.
- Sippel*: Monatschr. f. Geburtsh. u. Gynäk., xvii, 102.
- Stowe*: Surg., Gynec. and Obst., 1912, No. 1.
- Thomas*: Dissertation, Thèse de Paris, 1904.
- Traub*: Semaine gynéc., 1903, viii, 42.
- Veit*: Ges. f. Geburtsh. u. Gynäk., 1910, ii, 21, ref. Zentralbl. f. Gynäk., 1910, p. 779; Prakt. Ergebn. d. Geburtsh. u. Gynäk., 1910, iv.
- Vertes*: Monatschr. f. Geburtsh. u. Gynäk., xxiii, No. 2.
- Vineberg*: Am. Jour. Obst., 1916, lxxii, 288.
- Vincent*: Med. Brief, 1904, xxxii, 669, ref. Frommels Jahresb., 1904.
- Wormser*: Gynäk. Rundschau, 1909, No. 13.
- Wyder*: Korrespondenzbl. f. Schweizer Aerzte, 1910, No. 28.
- Zangemeister*: Ztschr. f. Geburtsh. u. Gynäk., 1908, lxii, No. 3 (Experimentelle Arbeit).

## Peritonitis

- Baisch*: München. med. Wehnschr., 1911, No. 38.  
*Bauer*: Arch. f. Chir., xvi, No. 4.  
*Bell*: Illinois Med. Jour., 1904, vi, 161, ref. Frommels Jahresb., 1904.  
*Benthin*: Zentralbl. f. Gynäk., 1919, No. 43; Med. Klin., 1921, Nos. 5 and 6; Monatschr. f. Geburtsh. u. Gynäk., lx.  
*Boerma*: Nederl. Tijdschr. v. Geneesk., 1908, ii, ref. Frommels Jahresb., 1908.  
*Bognet*: Arch. mens. d'obst. et de Gynéc., 1912.  
*Boquel*: Arch. méd. d'Angers, 1903, vii, 153, ref. Frommels Jahresb., 1903.  
*Broca*: Soc. de Chir. de Paris, 1912, x, 15, ref. Presse méd., No. 86.  
*Brinkley*: Virginia Med. Semi-Month., 1915, p. 10.  
*Bumm*: Strassburger Gyn.-Kongress, 1909.  
*Burtenshaw*: Jour. Am. Med. Assn., 1903, No. 15, p. 961.  
*Cardot*: Thèse de Paris, 1910.  
*Cooke-Hirst*: Am. Jour. Obst., June, 1912.  
*Derganě*: München med. Wehnschr., 1916, No. 5.  
*DuCoze*: Surg., Gynec. and Obst., 1921, xxxii, 299.  
*Dubs*: Schweizer med. Wehnschr., 1921, No. 3.  
*Ennicke*: Med. Klin., 1918, No. 45.  
*Federmann*: Berl. klin. Wehnschr., 1908, No. 28.  
*Franz*: Therap. d. Gegenw., 1912, No. 1.  
*Fromme*: Prakt. Ergenbn. d. Geburtsh. u. Gynäk.,  
*Ghrist*: Woman's Med. Jour., 1904, xiv, 26, ref. Frommels Jahresb., 1904.  
*Gilliani*: Jour. Am. Med. Assn., 1908, li.  
*Glimm*: Deutsch. Ztschr. f. Chir., 1906, lxxxiii.  
*Gueniot*: L'Obstetrique, 1905, x, 258; El consultor terapeutico, Paris, December, 1908, ref. Frommels Jahresb., 1908; Bull. Soc. d'Obst. de Paris, 1904, vii, 98.  
*Haselhorst*: München med. Wehnschr., 1922, No. 20, p. 766.  
*Hauch*: Ugesk. f. Laeger, 1916, No. 30; ref. Zentralbl. f. Gynäk., 1918, No. 5, p. 104.  
*Heimann*: Ztschr. f. Geburtsh. u. Gynäk., lxxi, No. 3.  
*Hirschel*: Bruns Beitr. z. klin. Chir., 1907, lvi; 39 Deutsch. Chirurgenkongress, 1910, Berlin, ref. Zentralbl. f. Gynäk., 1910, No. 20.  
*Hochne*: München med. Wehnschr., 1909, No. 49.  
*Hooch*: Dissertation, Basel, 1908, ref. Zentralbl. f. Gynäk., 1910, No. 24.  
*Hornstein*: Arch. f. Gynäk., xvii, No. 1.  
*Jeannin*: L'Obstetrique, 1906, xi, 5.  
*Katzenstein and Schulz*: Klin. med. Wehnschr., 1922, No. 11.  
*Kendal*: Maritime Med. News, 1905, xvii, 22, ref. Frommels Jahresb., 1905.  
*Kennedy*: Am. Jour. Obst., 1916, lxxiii, 801.  
*Kleine*: Dissertation, Berlin, 1920, ref. Zentralbl. f. Gynäk., 1920, No. 46.  
*Koblanck*: Strassburger Gyn.-Kongress, 1909; Ztschr. f. ärztl. Fortbild., 1912, No. 13; Monatschr. f. Geburtsh. u. Gynäk., 1.  
*Kownatzki*: Berl. med. Ges., 1905, vi, 28, ref. Berl. klin. Wehnschr., 1905, No. 30, p. 938.  
*Kritzler*: Zentralbl. f. Gynäk., 1909, No. 28.  
*Krönig*: Strassburger Gyn.-Kongress, 1909.  
*Kuhn*: Ztschr. f. Geburtsh. u. Gynäk., lxx; Arch. f. Chir., xvi, Nos. 3 and 4; München med. Wehnschr., 1911, No. 38.  
*Laeven*: Deutsch. ztschr. f. Chir., clxii, Nos. 1 and 2.  
*Latzko*: Wien. klin. Wehnschr., 1907, No. 19; Strassburger Gyn.-Kongress, 1909; Med. Klin., 1910, No. 24; Wien. med. Wehnschr., 1921, Nos. 45, 46, 49.  
*Leopold*: Zentralbl. f. Gynäk., 1908, No. 27; Strassburger Gyn.-Kongress, 1909; Arch. f. Gynäk., lxxviii, No. 1; *ibid.*, lxxxv, No. 3.  
*Lepage*: Compt. rend. Soc. d'obstet., de gynec. et de paediat. de Paris, 1905, vii; *ibid.*, 1905, vii, 131.

- Lienhard*: Schweizer med. Wehnschr., 1921, No. 29.  
*Masure*: Jour. de méd. de Paris, November, 1908; Gaz. gynéc., 1909.  
*Mauclaire*: Compt. rend. Soc. d'obstet., de gynéc. et de paediat. de Paris, 1905, vii.  
*Meyer*: Zentralbl. f. Gynäk., 1921, No. 10.  
*Müller*: Texas State Med. Jour., 1915, ii, 71.  
*Murat-Willis*: Surg. Gynec. and Obst., xxxiii, No. 4; ref. Zentralbl. f. Gynäk., 1922, No. 27, p. 1117.  
*Neudörfer*: Zentralbl. f. Chir., 1921, No. 1.  
*Nordmann*: Arch. f. Chir. lxxxix, No. 4.  
*Nösske*: 39 deutsch. Chirurgenkongress, 1910, Berlin, ref. Zentralbl. f. Gynäk., 1910, No. 20.  
*Noetzel*: Bruns Beitr. z. klin. Chir., lxxvii, No. 2.  
*Pfannenstiel*: Strassburger Gyn.-Kongress, 1909.  
*Payr*: Zentralbl. f. Chir., 1922, No. 1.  
*Polak*: Am. Jour. Obst., 1918, lxxviii, 916; Am. Jour. Obst. and Gynec., 1920, i, 161.  
*Pryor*: New York Med. Jour., 1904, lxxix, 155.  
*Reschke*: Arch. f. Chir., cxvi, No. 3.  
*Robb*: Am. Gynec., 1903, ii, No. 6.  
*Ross*: Am. Jour. Obst., 1908, lviii.  
*Rotter*: Arch. f. Chir., xciii, No. 1; Freie Vereinigung der Chirurgen, Berlin, 1909, xii, 13, ref. Deutsch. med. Wehnschr., 1910, No. 11, p. 529, Discussion, ibid., No. 12, p. 586.  
*Rouffart*: Jour. de chir. et ann. Soc. belge de chir., 1906, No. 2, ref. Frommels Jahreshb., 1906.  
*Schmerz*: München med. Wehnschr., 1921, No. 13.  
*Sellheim*: Berl. Klin., 1907, p. 231.  
*Seubert*: München med. Wehnschr., 1918, No. 52.  
*Sherill*: Am. Jour. Obst., February, 1905, li, 275.  
*Sigwart*: Arch. f. Gynäk., xcix, 100, 103; München med. Wehnschr., 1922, No. 14.  
*Sourdille*: Compt. rend. Soc. d'obstet. de gynéc. et de paediat. de Paris, 1905, vii, 40-48; Rev. de gynéc. et de chir. abd., 1905, ix, No. 5.  
*Stoeckel*: Med. Gesellsch. zu Kiel, July, 1912, ref. München. med. Wehnschr., 1912, p. 2133.  
*Veit*: Monatschr. f. Geburtsh. u. Gynäk., xxxvi, Erg.-H.  
*Vignard and Ormand*: Lyon chir., v.  
*Weber*: München med. Wehnschr., 1921, No. 8, p. 254.  
*Wolfsohn*: München med. Wehnschr., 1918, No. 49.  
*Zesas*: Zentralbl. f. d. Grenzgeb. d. inn. Med. u. Chir., xv.

### Ligation of Veins

- Antoine*: Dissertation, Halle, 1909.  
*Asch*: Sitzungsber., Berl. klin. Wehnschr., 1913, p. 134.  
*Baldwin*: Am. Jour. Obst., 1915, lxxi, 292; Am. Jour. Obst. and Gynec., 1923, v, No. 5.  
*Bardleben*: Berl. klin. Wehnschr., 1908, No. 6; Arch. f. Gynäk., lxxxiii, Nos. 1 and 2.  
*Bencke*: Verein mitteldeutsch. Gynäk., 1912, i, 21, ref. Zentralbl. f. Gynäk., 1912, p. 334.  
*Benthin*: Zentralbl. f. Gynäk., 1912, No. 39.  
*Berkofsky*: Deutsch. med. Wehnschr., 1908, No. 17.  
*Beuthner*: Soc. méd. de Genève, 1911, ii, 9, ref. Frommels Jahreshb., 1911.  
*Birnbaum*: Arch. f. Gynäk., lxxiv, No. 1, cxiv, No. 3.  
*Blair-Bell*: Practitioner, 1911; Brit. Med. Jour., 1921, No. 3150.  
*Brix*: München med. Wehnschr., 1913, No. 24.  
*Brown*: Med. Record, New York, 1914, lxxxv, No. 19.



- Bumm:* Gesellsch. d. Charité-Aerzte, 1904, xi, 17, ref. Deutsch. med. Wehnschr., 1904, No. 52, Vereinsbeilage, p. 1947; Berl. med. Ges., 1905, iii, 18, ref. München med. Wehnschr., 1905, No. 28; Semaine méd., 1905, No. 19; Med. Blätter, Wien, 1905, No. 28; Strassburger Gyn.-Kongress, 1909.
- Cuff:* Jour. Obst. and Gynec., Brit. Emp., 1906, ix.
- Doederlein:* Zentralbl. f. Gynäk., 1908, No. 24, p. 797; Zentralbl. f. Gynäk., 1908, No. 39; Ibid., 1915, p. 55.
- Fair:* Bull. Soc. d'Obst. de Paris, 1906, No. 9; Gaz. hôp. de Paris, 1907, lxx.
- Falk:* Geburtsh. Ges. Hamburg, 1907, x, 8, ref. Zentralbl. f. Gynäk., 1908, p. 104.
- Freund:* Deutsch. med. Wehnschr., 1908, No. 39, p. 1702, Sitzungsber.
- Friedemann:* München med. Wehnschr., 1906, No. 37; Zentralbl. f. Gynäk., 1908, No. 23.
- Fromme:* München med. Wehnschr., 1907, pp. 241 and 1059; Ztschr. f. Geburtsh. u. Gynäk., lxxvi, No. 2; Verein mitteldeutsch. Gynäk., 1912, i, 21, ref. Zentralbl. f. Gynäk., 1912, p. 331; Prakt. Ergebn. d. Geburtsh. u. Gynäk., i.
- Gillmore:* Jour. Am. Med. Assn., June 21, 1913, No. 25.
- Glück:* Chirurgenkongress, 1880.
- Guiccardi:* Ann. di ostet. e gin., 1906, No. 1, ref. Zentralbl. f. Gynäk., 1908, p. 865.
- Graefe:* Verein mitteldeutsch. Gynäk., 1912, i, 21; ref. Zentralbl. f. Gynäk., 1912, p. 334.
- Grube:* Geburtsh. Ges. Hamburg, 1907, x, 8, ref. Zentralbl. f. Gynäk., 1908, p. 104.
- Gwathurney:* Virginia Med. Semi-Month., 1905-1906, x, ref. Frommels Jahresb., 1906.
- Haeckel:* Deutsch. med. Wehnschr., 1905, No. 41.
- Hammerschlag:* Gynäk.-Ges., Berlin, 1910, vi, 24, ref. Zentralbl. f. Gynäk., 1911, p. 417.
- Hartmann:* Berl. klin. Wehnschr., 1911, No. 12.
- Henckel:* Verein mitteldeutsch. Gynäk., 1912, i, 21, ref. Zentralbl. f. Gynäk., 1912, p. 333; Strassburger Gyn.-Kongress, 1909.
- Herzog:* Berl. klin. Wehnschr., 1909, No. 20; Surg., Gynec. and Obst., xxv, 452.
- Hoehne:* Med. Ges. z. Kiel, July, 1912, ref. München med. Wehnschr., 1912, p. 2134.
- Jellet:* Surg., Gynec. and Obst., xvii, No. 2.
- King:* Interstate Med. Jour., 1914, xxxi; Jour. Am. Med. Assn., July, 1920.
- Koblanck:* Ztschr. f. Geburtsh. u. Gynäk., lxiv, No. 3.
- Kownatzki:* Berl. klin. Wehnschr., 1905, No. 30; Die Beckenvenen, Bergmann, Wiesbaden, 1907.
- Kraussold:* Arch. f. Chir., xxii.
- Latzko:* Wien. med. Wehnschr., ibid., 1907, No. 19, p. 553; ibid., 1909, No. 27; Strassburger Gyn.-Kongress, 1909; Med. Klin., 1910, No. 24.
- Lee:* Med. Times, 1865.
- Lejars:* XIX. Congress de Chir., 1906, p. 469, ref. Frommels Jahresb., 1906.
- London:* Australasian Med. Gaz., 1907, xxvi, ref. Frommels Jahresb., 1907.
- Lenhartz:* Med. Klin., 1906, p. 160; Nothnagels spez. Path. u. Therap., iii, Part IV, No. 1.
- Leopold:* Zentralbl. f. Gynäk., 1905, No. 13; Zentralbl. f. Gynäk., 1908, No. 24; Arch. f. Gynäk., lxxxix, No. 1; Gynäk. Ges. Dresden, 1909, xi, 18, ref. Zentralbl. f. Gynäk., 1910, p. 379.
- Lomer:* Geburtsh. Ges. Hamburg, 1907, x, 8, ref. Zentralbl. f. Gynäk., 1908, p. 104.
- Martens:* Arch. f. Chir., cxvi, No. 4.
- Menge:* Strassburger Gyn.-Kongress, 1909.

- Michels*: Lancet, London, 1903, i, 1025, *ibid.*, 1909, ii, 1656.  
*Miller*: Jour. Am. Med. Assn., July, 1917.  
*Moore*: Intercolonial Med. Jour. Australasia, 1907, xii, ref. *Frommels Jahresb.*, 1907.  
*Noble*: Zentralbl. f. Gynäk., 1909, No. 12, p. 420.  
*Nyulsay*: Surg. Gynec. and Obst., xxx, No. 3.  
*Opitz*: Deutsch. med. Wehnschr., 1904, Nos. 25 and 26; *ibid.*, 1905, No. 50; Strassburger Gyn.-Kongress, 1909.  
*Osterloh*: Gynäk. Ges. z. Dresden, 1909, xi, 18, ref. Zentralbl. f. Gynäk., 1910, p. 379.  
*Praetorius*: Ges. d. Charité-Aerzte, 1908, vii, 16, ref. Deutsch. med. Wehnschr., 1908, No. 39, p. 1699.  
*Prochownik*: Geburtsh. Ges. Hamburg, 1907, x, 8, ref. Zentralbl. f. Gynäk., 1908, p. 104; *ibid.*, 1908, No. 4.  
*Resinelli*: La Ginecologie, 1908, xviii, 560, Firenze, ref. *Frommels Jahresb.*, 1910.  
*Schergoff*: Dissertation, Berlin, 1904.  
*Schwyzer*: Surg., Gynec. and Obst., xx, No. 4.  
*Seeligmann*: Geburtsh. Ges. Hamburg, 1907, x, 8, ref. Zentralbl. f. Gynäk., 1908, p. 104.  
*Seitz*: Volkmanns Sammlg. klin. Vortr., No. 171; Monatsschr. f. Geburtsh. u. Gynäk., xxvi, 493; München med. Wehnschr., 1906, No. 52, p. 2585; Volkmanns Sammlg. klin. Vortr., N. F. No. 464.  
*Simpson*: Lancet, London, 1903, i, 1199.  
*Süssmann*: Orvoskepes, 1921, Festschr. f. Tauffer, ref. Zentralbl. f. Gynäk., 1922, No. 6.  
*Stewart*: Am. Jour. Obst., 1906, liv, 224.  
*Taylor*: Brit. Gynec. Jour., 1905, xxi; Birmingham Med. Rev., 1905, lvii, ref. *Frommels Jahresb.*, 1905.  
*Thorn*: Verein mitteldeutsh. Gynäk., 1912, i, 21, ref. Zentralbl. f. Gynäk., 1912, p. 332.  
*Trendelenburg*: München med. Wehnschr., 1902; Jour. Am. Med. Assn., July, 1906.  
*Vauverts and Paucot*: Presse méd., 1912, p. 967.  
*Veit*: Verein mitteldeutsh. Gynäk., 1912, i, 21, ref. Zentralbl. f. Gynäk., 1912, p. 331; Berl. Gynäk. Ges., 1913.  
*Venus*: Zentralbl. f. d. Grenzgeb. d. inn. Med. u. Chir., 1911, No. 14ff.  
*Warnekros*: Arch. f. Gynäk., xevii, No. 1.  
*Weydling*: Zentralbl. d. Ver. deutsch. Aerzte in Reichenberg, xxiii, No. 4.  
*Williams*: Am. Jour. Obst., 1909, lxi.  
*Wormser*: Med. Klin., 1908, No. 19; Gynäk. Rundschau, 1909, No. 15.

## Disinfectants

### (a) Corrosive Sublimate

- Alvarez and Enriquez*: Ann. de la accad. de obst., etc., Madrid, 1910, iii, 329, ref. *Frommels Jahresb.*, 1910.  
*Antonelli*: Policlinico, 1911.  
*Barszony*: Obstetrique, November, 1909; Budapest. kgl. Aerzteverein, Sitzungsber., 1911, xi, 25, ref. Orvosi Hetilap, 1911, No. 52.  
*Encrnao*: Policlinico, 1911.  
*Fabio*: Gaz. degli osped. e delle cliniche, Milano, 1904, No. 49, p. 519; Riv. di Ostet., Ginec. e pediatr., Roma, 1905, ix, 214.  
*Grandoni*: Policlinico, 1911.  
*Hochhalt*: Sitzungsber. d. Budapest. Spitalsärzte, 1910, xi, 2, ref. Orvosi, Hetilap, 1911, No. 2.  
*Hüssy*: Zentralbl. f. Schweizer Aerzte, 1911; Gynäk. Rundschau, 1911, No. 8.  
*Kalledey*: Orvosi Hetilap, 1911, No. 2.  
*Keneczy*: Orvosi Hetilap, 1911, No. 52.

- Mariani:** Policlinico, 1903, Gaz. deli osped., 1903; Win. klin-therap. Wehnschr., 1903, Nos. 47 and 48.
- Pende:** Riv. di Ostet., Ginec. e pediatri., Roma, 1905, vi, 169.
- Piper:** Am. Jour. Obst. and Gynec., 1922, iv, 532 (see discussion by Hirst and McGlynn); Surg. Clin. North America, 1924, iv, 177.
- Pollizotti:** Ann. di Ostet., Ginec., Milano, anno, xxxii, ii, No. 9.
- Robin:** Rev. Internat. de méd. et de chir., Paris, 1905, xvi, 167.
- Rossi:** Policlinico, 1911.
- Schklavsky:** Russki Wratsch, 1913, No. 20, ref. Frommels Jahresb., 1913.
- Schmidlechner:** Orvosi Hetilap, 1911, No. 51, p. 1471.
- Souligoux:** Bull. Soc. de chir., Paris, 1912.
- Stowe:** Am. Jour. Obst., 1909, lx; Surg., Gynec. and Obst., 1912, No. 1.
- Turnminna,** Morgagni, lv, No. 8.

(b) *Magnesium Sulphate, Formalin, Iodine, etc.*

- Barrow:** Med. Record, New York, 1903, lxiii, 158; Am. Jour. Obst., 1903, xlvii, No. 3, p. 366; New York Obst. Assn., 1903, i, 13; Am. Gynec., 1903, No. 3, p. 264; New York Med. Jour., 1903.
- Bauer:** Med. Record, New York, 1903, lxiii.
- Becker:** Zentralbl. f. Gynäk., 1921, No. 34.
- Brodhead:** Am. Jour. Obst., 1903, xlvii.
- Copeland:** Surg., Gynec. and Obst., 1920, Abst., xxx, 56.
- Ducrocq:** New Orleans Med. and Surg. Jour., 1903, lvi, 18, ref. Frommels Jahresb., 1903.
- Dudley:** Am. Jour. Obst., 1903, xlvii.
- Editorial,** Ann. of Gynec., April, 1903, p. 236; New York Med. Record, 1903, lxiii.
- Elbrech and Snoddergras:** Am. Gynec., 1903, No. 86, ref. Frommels Jahresb., 1903.
- Fanoni:** Post-Graduate New York, 1903, xviii, 520.
- Fortescu-Brickdale:** Lancet, London, 1903, i, 98.
- Gilley:** Med. Century, 1903, xi, 230.
- Goldhorn:** Proc. New York Path. Soc., 1903-1904, iii, 26.
- Green:** Med. News, 1903, x, 10.
- Hamblin:** Am. Med. Month., 1904, xxi, 279.
- Harrar:** Am. Jour. Obst., lxviii, 825.
- Hill:** Med. Record, New York, 1903, lxiii.
- Hoerschelmann:** Petersburger med. Wehnschr., 1904, p. 33.
- Honan:** Homoeop. Jour. Obst., 1903, xxv, 79, ref. Frommels Jahresb., 1903.
- Huggins:** Am. Jour. Obst., February, 1911, Med. Record, New York, 1914, lxxxv, No. 19.
- Ilkewitch:** Zentralbl. f. Gynäk., 1913, p. 1399.
- Killiani:** Am. Jour. Obst., 1903, xlvii.
- Koehler:** Zentralbl. f. Gynäk., 1916, No. 39.
- Lindig:** Med. Klin., 1921, No. 23.
- Mahnert and Sautner:** Arch. f. Gynäk., cxvi, No. 1.
- Marx:** Jour. Obst., 1903, xlvii.
- Michael:** Klin. Wehnschr., 1922, No. 23.
- Nelson:** New York Med. Jour., 1903, lxxvii, 613.
- Park:** Johns Hopk. Hosp. Bull., 1903.
- Park and Payne:** Med. Record, New York, 1903, lxiii, 299; Proc. New York State Soc., 1903-1904, iii, 23.
- Polk:** Med. Record, New York, 1903, lxiii.
- Pryor:** Am. Jour. Obst., 1903, xlvii.
- Schmerz:** München med. Wehnschr., 1921, No. 23.
- Schneichel:** Dissertation, Hamburg, 1922, ref. Zentralbl. f. Gynäk., 1922, No. 49, p. 1981.
- Schwarzenbach:** Zentralbl. f. Schweizer Aerzte, 1905.
- Shaw:** Jour. of Hygiene, April, 1903.
- Smythe:** Memphis Med. Month., 1903, xxiii, 150, ref. Frommels Jahresb., 1903.

- Steele*: Lancet, London, 1903, ii, 1163.  
*Stone*: Am. Jour. Obst., 1903, xlvii.  
*Vineberg*: Am. Jour. Obst., 1903, xlvii.  
*Waitsfelder*: Med. Record, New York, 1903, lxiii, 974.  
*Waldo*: Am. Jour. Obst., 1903, xlvii.  
*Williams*: Med. Record, New York, 1903, lxiii.

### Silver Preparations

(*Dyes, Collorgol, Electrorgol, Methylene Blue Silver, Acridin Preparations, etc.*)

- Albrecht*: Gynäk. Ges. München, 1909, vi, 17, ref. Zentralbl. f. Gynäk., 1909.  
*Alcosta*: Arch. de ginec., Barcelona, xxii, 266, ref. Frommels Jahresb.  
*Aron*: Deutsch. med. Wehnschr., 1920, No. 35.  
*Auboyer*: Thèse de Paris, 1908.  
*Audebert*: Ann. Soc. d'Obst. de France, Session X, 1904, p. 231; Jour. d'accouch., Liège, 1904, viii, 14, ref. Frommels Jahresb., 1904.  
*Bamberger*: Berl. klin. Wehnschr., 1903, No. 34.  
*Baros*: Rev. méd. de l'est, Nancy, 1907, xxxix, ref. Frommels Jahresb., 1907.  
*Bauereisen*: Zentralbl. f. Gynäk., 1921, No. 34.  
*Baum*: Gynäk. Ges. Breslau, 1905, v, 16, ref. Zentralbl. f. Gynäk., 1905, No. 46, p. 1425.  
*Baylac*: Arch. méd. de Toulouse, 1903, ix, 136, ref. Frommels Jahresb., 1903.  
*Bechhold*: München med. Wehnschr., 1922, No. 41.  
*Becker*: Zentralbl. f. Gynäk., 1921, No. 34.  
*de Benjoa*: El siglo med., Madrid, 1909, xii, 11, ref. München med. Wehnschr., 1910, No. 7.  
*Billinghurst*: Buenos Ayres, Argentina Medica, 1910, ii, 13, ref. Frommels Jahresb., 1910.  
*Blaise*: Nederl. Tijdschr. v. Geneesk., 1908, ii, 659, ref. Frommels Jahresb., 1908.  
*Bochanski*: Jour. Am. Med. Assn., 1922, lxxix, 1808.  
*Böckelmann*: Deutsch. med. Wehnschr., 1906, No. 26.  
*Boehring*: Ztschr. f. Wundärzte u. Geburtsh., 1904, iv, 190.  
*Boettner*: München med. Wehnschr., 1921, No. 28; Arch. f. klin. med., cxxv.  
*Bohlandt*: Deutsch. med. Wehnschr., 1919, No. 29; Med. Klin., 1919, No. 46.  
*Boissard and Verdoux*: Soc. d'Obst. de gynec. et de paediat. de Paris, 1916, ref. Zentralbl. f. Gynäk., 1916, p. 1059.  
*Bong*: Therap. Monatschr., October, 1903.  
*Bonnaire*: Presse méd., 1906, No. 93; Rev. medical, 1906, xi, 21; Internat. Clin., 1907, iii, 170, ref. Frommels Jahresb., 1907.  
*Bonnaire and da Costa*: Movimento med., Coimbra, 1905-1906, v, ref. Frommels Jahresb., 1906.  
*Bonnaire and Jeannin*: L'Obstetrique, April, 1908; ibid., 1910, ref. Zentralbl. f. Gynäk., 1910, p. 1084.  
*Borchardt*: Dissertation, Leipzig, 1903.  
*Bossan and Marcellet*: Gaz. d. hôp., 1908, No. 103.  
*Bossart*: Zentralbl. f. Schweizer Aerzte, 1910, No. 23.  
*Breton*: Rev. gén. de chir. et de therap., 1905, xix, ref. Frommels Jahresb., 1903.  
*Buberl*: Wien. klin. Wehnschr., 1906, No. 10.  
*Caldesi*: Ann. di obstet. e ginec., Milano, 1908, xxx.  
*Camerer*: Therap. d. Gegenw., February, 1904.  
*Capitan*: Compt. rend. Soc. de biol., 1907, lxii.  
*Carnus*: Thèse de Paris, 1905.  
*Castro-Peizoto*: Brazil-med., Rio de Jan., 1907, xxi, ref. Frommels Jahresb., 1907.  
*Caudet*: Thèse de Paris, 1910.



- Cealic and Dimitrin*: Rev. de chir., Bucureste, 1905, ix, ref. Zentralbl. f. Gynäk., 1905, No. 40, p. 1227.
- Cernovodeanu and Henri*: Compt. rend. Soc. de biol., 1906, lxi, 122.
- Chassevant and Pasternak*: Compt. rend. Soc. de biol., 1903, lv, 433.
- Ciffer*: Nederl. Tijdschr. v. Geneesk., 1908, ii, 767, 985, ref. Frommels Jahresb., 1908.
- Coblentz*: Therap. Gaz., 1903, xix, 526, ref. Frommels Jahresb., 1903.
- Cohen*: St. Louis Med. Rev., 1906, liii.
- Cohn, E.*: Berl. klin.-therap. Wehnschr., 1905, p. 63.
- Cohn*: Rev. de chir., Bucureste, June, 1906, ref. Zentralbl. f. Gynäk., 1906, No. 45; Rev. de chir., Bucureste, August, 1908, ref. Zentralbl. f. Gynäk., 1909, No. 12, p. 419; Rev. de chir., Bucureste, April, 1913, ref. Zentralbl. f. Gynäk., 1914, p. 1270.
- de Coster*: Arch. méd. belge, Brux., 1907, series 4, xxx, 301, ref. Frommels Jahresb., 1908.
- Coudrat-Desvergnès*: Thèse de Bordeaux, 1908, ref. Frommels Jahresb., 1908.
- Coudray*: Progrès méd., 1903, xvii, 81.
- Corminas*: Rev. de cien. méd. de Barcelona, 1903, xxix, 49, ref. Frommels Jahresb., 1903; Rev. de med. y cirug. práct., Madrid, 1904, No. 820, ref. Frommels Jahresb., 1904.
- Courant*: Gynäk., Ges. Breslau, 1905, ii, 16, ref. Zentralbl. f. Gynäk., 1905, No. 46, p. 1425.
- Credé*: Ztschr. f. ärztl. Fortbild., 1904, No. 20; Arch. f. klin. Chir., lxi, 225; München med. Wehnschr., 1906, No. 24.
- Daels*: Zentralbl. f. Gynäk., 1913, p. 329.
- Decker*: Dissertation, Bonn, 1910.
- Dessoutier*: Méd. orient., Paris, 1907, xi, ref. Frommels Jahresb., 1907.
- Dietrich*: Zentralbl. f. Gynäk., 1921, No. 45.
- Dührssen*: München med. Wehnschr., 1922, No. 14.
- Dunger, R.*: Deutsch. Arch. f. klin. Med., li.
- Ebeler*: Monatschr. f. Geburtsh. u. Gynäk. xlviii, No. 4.
- Ehrlich*: Ztschr. f. ärztl. Fortbild., 1909.
- Eisenberg*: Berl. klin. Wehnschr., 1911, No. 36.
- Eisenreich*: Gynäk. Ges. München, 1909, vi, 17, ref. Zentralbl. f. Gynäk., 1909.
- Eufinger*: München med. Wehnschr., 1923, No. 4.
- Exner*: Wien. klin. Wehnschr., 1921, No. 4.
- Falkner*: Geburtsh. u. Gynäk. Ges. in Wien, 1905, xi, 30, ref. Zentralbl. f. Gynäk., 1906, No. 9, p. 250.
- Ferreira de Silva*: Ann. acad. de med., Rio de Janeiro, 1906, lxx, ref. Frommels Jahresb., 1907.
- Fleischer*: Russky Wratsch. 1907, No. 37, ref. Frommels Jahresb., 1907.
- Fortescue-Brickdale*: Bristol Med. and Chir. Jour., December, 1903, p. 337.
- Fuhmann*: Monatschr. f. Geburtsh. u. Gynäk., xliii, No. 4.
- Ganz*: Therap. Monatschr., 1906, p. 140.
- Gastongway*: Bull. med. de Quebec, 1905-1906, vii, 145-151, ref. Frommels Jahresb., 1906.
- v. Gaza*: Klin. Wehnschr., 1922, No. 16.
- Georgi*: Ztschr. f. ärztl. Fortbild., 1904, No. 20.
- Da Giaca*: Gaz. clin., S. Paulo, 1905, iii, 430, ref. Frommels Jahresb., 1905.
- Gompel and Henry*: Compt. rend. Soc. de biol., 1906, lxi.
- Guerin*: Jour. de méd. de Bordeaux, 1903, i, 33, p. 845, ref. Frommels Jahresb., 1903.
- Guilloz*: Rev. méd. de l'Est, Nancy, 1903, xxxv, 282, ref. Frommels Jahresb., 1903.
- Haack*: Nordostdeutsche Ges. f. Gynäk., 1908, xi, 28, ref. Deutsch. med. Wehnschr., 1909, No. 11.
- Hachtmann*: Dissertation, Halle a S., 1920.

- Hadges*: Jour. d'accouch. de Liège, 1904, xxv, 244, ref. *Frommels Jahreshb.*, 1904.
- Hadra*: Pommersche gyn. Ges., 1907, v, 12, ref. *Monatschr. f. Geburtsh. u. Gynäk.*, xxvi, 272.
- Harrison*: Med. Record, New York, 1903, liv; *Virginia Med. Semi-Month.*, 1903, viii, 477, ref. *Frommels Jahreshb.*, 1903; *New York State Jour. Med.*, 1904, iv, 184.
- Hartwig*: Deutsch. med. Wehnschr., 1920, No. 51.
- Haushalter*: Rev. méd. de l'Est, Nancy, 1903, xxxv, 276, ref. *Frommels Jahreshb.*, 1903.
- Heimann*: Ztschr. f. Geburtsh. u. Gynäk., lxxi, No. 3.
- Hekimoglou*: Rev. gén. de clin. et de thérap., 1907, xxi, ref. *Frommels Jahreshb.*, 1907.
- Hénrard*: Monatschr. f. Geburtsh. u. Gynäk., lx.
- Herschman*: Monatschr. f. Geburtsh. u. Gynäk., lxiii, Nos. 4 and 5.
- Hocheisen*: Med. Klin., 1906, Nos. 31-34.
- van der Hoeven*: Niederl. gyn. Ges., 1907, xi, 17, ref. *Zentralbl. f. Gynäk.*, 1908, p. 109.
- Hoffmann*: Dissertation, Leipzig, 1908.
- Hotz and Winterberg*: Allg. med. Centr.-Ztg., 1905, lxxiv, 879.
- Hoummel*: Presse méd., 1906, No. 2.
- Hüssy*: München med. Wehnschr., 1915, No. 17, and Ztschr. f. Geburtsh. u. Gynäk., lxxxvi.
- Jaenike*: Deutsch. med. Wehnschr., 1903, No. 6.
- Jeannin*: Progrès méd., August, 1908.
- Jötten*: Arch. f. Gynäk., cvii, No. 1.
- Jousset*: Compt. rend. Soc. de biol., 1903, lv, 943.
- Katzenstein and Schulz*: Klin. Wehnschr., 1922, No. 11.
- Kausch*: Arch. f. Chir., cii, No. 4; *Deutsch. med. Wehnschr.*, 1912, No. 35.
- Kirchhoff*: Dissertation, Marburg, 1911; Ztschr. f. Geburtsh. u. Gynäk., lxxi, No. 3.
- Klapp*: Deutsch. med. Wehnschr., 1921, No. 46.
- Klauhammer*: München med. Wehnschr., 1913, No. 14.
- Klein*: Berl. med. Wehnschr., 1905, No. 3.
- Klotz*: Gynäk. Ges. Dresden, 1902, v, 15, ref. *Zentralbl. f. Gynäk.*, 1903, No. 18, p. 554.
- Kochler*: Zentralbl. f. Gynäk., 1912, No. 56.
- Krauss*: Geburtsh. u. Gynäk. Ges. in Wien, 1906, ii, 20, ref. *Zentralbl. f. Gynäk.*, 1906, No. 40, p. 1102.
- Krüll*: Gynäk. Ges. Dresden, 1902, v, 15, ref. *Zentralbl. f. Gynäk.*, 1903, No. 18, p. 554.
- Kühnelt*: Zentralbl. f. Gynäk., 1916, No. 32.
- Latzel*: Wien. klin. Wehnschr., 1923, No. 26.
- Le Calve*: Gaz. méd. de Nantes, 1908, viii, 29, ref. *Frommels Jahreshb.*, 1908.
- Legrand*: Thèse de Paris, 1904.
- Leopold*: Gynäk. Ges. Dresden, 1902, v, 15, ref. *Zentralbl. f. Gynäk.*, 1903, No. 18, p. 554.
- Leschke*: Berl. klin. Wehnschr., 1920, No. 4.
- Lichtenauer*: Pommersche Gesselsch. f. Gynäk., 1907, v, 12, ref. *Monatschr. f. Geburtsh. u. Gynäk.*, xxvi, 272.
- Lindig*: Med. Klin., 1921, No. 13.
- Loebl*: Wien. klin. Wehnschr., 1903, No. 44; *Therap. d. Gegenw.*, 1904, xix, No. 4, p. 152.
- Loeser*: Zentralbl. f. Gynäk., 1918, No. 40.
- Loewe*: Berl. med. Wehnschr., 1905, No. 3, p. 162.
- Maertens*: Jour. d'accouch., Liège, 1908, xxix, 271.
- Makelaire*: Spitalul, 1909, No. 11, ref. *Zentralbl. f. Gynäk.*, 1909, p. 333.
- Marsfeld*: Wien. klin. Wehnschr., 1918, No. 32.

- Marschner*: Gynäk. Ges. Dresden, 1902, v, 15, ref. Zentralbl. f. Gynäk., 1903, No. 18, p. 554.
- Meurer*: Niederl. gyn. Ges., 1907, xi, 17, ref. Zentralbl. f. Gynäk., 1908, p. 109.
- Michael*: Klin. Wehnschr., 1922, No. 23.
- Morgenroth*: Deutsch. med. Wehnschr., 1919, No. 19; Klin. Wehnschr., 1922, No. 8.
- Nejeloſſ*: Ztschr. f. Geburtsh. u. Gynäk. (russ.), October, 1906, ref. Frommels Jahresb., 1906.
- Netter*: Presse méd., 1903, No. 6, p. 91; Union méd. du Canada, Montreal, 1908, xxxvii, ref. Frommels Jahresb., 1908.
- Netter and Salomon*: Presse méd., 1903, No. 12, p. 157.
- Nijhoff*: Niederl. gyn. Ges., 1907, xi, 17, ref. Zentralbl. f. Gynäk., 1908, p. 109.
- Noire*: Presse méd., 1920, No. 37.
- Nyolow*: Jour. f. Geburtsh. u. Gynäk. (russ.), 1906, Nos. 8-12, ref. Zentralbl. f. Gynäk., 1908, p. 109.
- Osterloh*: Gynäk. Ges. Dresden, 1902, v, 15, ref. Zentralbl. f. Gynäk., 1903, No. 18, p. 554; Jahresb. d. Ges. f. Natur. u. Heilkunde, 1904-1905; Deutsch. Arch. f. klin. Med., 1905, lxxxv.
- Pasqueron*: Thèse de Paris, 1904.
- Pastia*: La presse méd., 1910, No. 27, p. 714.
- Patein*: Jour. de méd. de Bordeaux, 1910, xl, 365, ref. Frommels Jahresb., 1910.
- Pedraja and Tanago*: Il siglio med., Madrid, 1908, ref. Frommels Jahresb., 1908.
- Pinel*: Thèse de Toulouse, 1904, ref. Frommels Jahresb., 1904.
- Porak*: Ann. Soc. d'obstet. de France, X. Session, 1904, p. 231.
- Pranter*: Wien. klin. Wehnschr., 1921, No. 4.
- Rau*: Therap. Monatschr., December, 1905.
- Reichmann*: München med. Wehnschr., 1915, No. 20; Ibid., 1915, No. 56.
- Reverdin and Massol*: Rev. méd. de la Suisse rom., 1905, i, 20, p. 5.
- Ribadeau, Dumas and Bailleul*: Rev. génér. de clin. et de therap., Paris, 1905, xix, 231, ref. Frommels Jahresb., 1905.
- Rodewicz*: Ztschr. f. ärztl. Fortbild., 1904, No. 20.
- Rolly*: München med. Wehnschr., 1923, No. 5.
- Rommel*: Therap. Monatschr., October, 1903.
- Rooseu*: Deutsch. med. Wehnschr., 1914, No. 10 and 1917, No. 18.
- Rosenstein*: Therap. Monatschr., 1903, p. 343; Deutsch. med. Wehnschr., 1921, No. 44.
- Roux and Gainard*: Bull. méd. de l'Algerie, Algier, 1908, xix, ref. Frommels Jahresb., 1908.
- Ruckert*: Ges. f. Geburtsh. u. Gynäk., 1910, vi, 24, ref. Zentralbl. f. Gynäk., 1911, p. 415.
- Saalfeldt*: Zentralbl. f. Gynäk., 1917, No. 23.
- Schmid, H.*: New England Med. Month., 1903, xxii, 341, ref. Frommels Jahresb., 1903.
- Schmidt*: Deutsch. med. Wehnschr., 1903, No. 16, p. 13.
- Seidel*: Deutsch. med. Wehnschr., 1908, No. 31.
- Siebrecht and Ujheiyi*: Deutsch. med. Wehnschr., 1922, No. 15.
- Siegel*: Ztschr. f. Geburtsh. u. Gynäk., lxxxii, No. 3.
- Simon*: Rev. méd. de l'Est, 1903, xxxv, 275.
- Spielmann*: Rev. méd. de l'Est, 1903, xxxv, 275.
- Spiro*: Biochem. Ztschr., lxxiv.
- Stejskal*: Monographie, Wien, 1922, Safar.
- Stowe*: Surg., Gynec. and Obst., 1912, No. 1.
- Szťahovsky*: Pest. med.-chir. Presse, 1903, xxxix.
- Thenveny*: La med. Pratique, February, 1907; Bull. génér. therap., 1909, iv, 30, vol. clvii.

- Thiess*: Zentralbl. f. Gynäk., 1922, No. 31, p. 1282.  
*Torres Alonso*: Rev. de med. y cirurg. pract., Madrid, lxxxviii, ref. München med. Wehnschr., 1910, No. 44.  
*Trembur*: Naturwissenschaftl. med. Ges. zu Jena, 1909, i, 19, ref. München med. Wehnschr., 1909, p. 559.  
*Vale*: Am. Jour. Med. Sc., 1906, cxxxi, 725, ref. Frommels Jahresb., 1906.  
*Vauters*: Dissertation, Lille, 1909, ref. Zentralbl. f. Gynäk., 1911, p. 725.  
*Viett*: Aerztl. Rundschau, 1907, xvii, No. 19.  
*Voigt*: Ref. Deutsch. med. Wehnschr., 1914, p. 1596; Zentralbl. f. Gynäk., 1922, No. 16.  
*Vollert*: Therap. Neuheiten, Leipzig, 1906, i, 103.  
*Wassmuth*: Deutsch. med. Wehnschr., 1905, p. 1958; Ibid., 1906, No. 49.  
*Weidler*: Gynäk. Ges. Dresden, ref. Zentralbl. f. Gynäk., 1905, No. 13, p. 402.  
*Weissmann*: Therap. Monatsch., 1905; Ibid., 1907; Ibid., August, 1908; Therap. Rundschau, 1908, ii.  
*Wilke*: Heilkinde, 1906, p. 539; ibid., 1907, p. 138.  
*Wolf*: Deutsch. med. Wehnschr., 1913, p. 944.  
*Wolfson*: München med. Wehnschr., 1909, No. 27.  
*van Zandt*: Texas State Jour. Med., 1906-1907, ii, ref. Frommels Jahresb., 1907; Med. Era, 1910, xix, 238, ref. Frommels Jahresb., 1910.  
*Zieler and Birnbaum*: München med. Wehnschr., 1922, No. 18.

### Leucostimulants

- Audebert*: Soc. d'obstet. de Toulouse, L'Obstetrique, 1910, ii.  
*Bardenheuer*: Ziegler's Beitr., 1891.  
*Boissard*: L'Obstetrique, October, 1908; Ibid, 1910, No. 2.  
*Bröse*: Deutsch med. Wehnschr., 1904, No. 44.  
*Busse*: Arch. f. Chir., lxxv.  
*Bumm*: Berl. klin Wehnschr., 1905, No. 27.  
*Carnus*: Thèse de Paris, 1905.  
*Cazanore*: Compt. rend. Soc. d'obstet. et de gynéc. et de paediat. de Paris, 1909, xi, 382; Soc. d'obstet., L'Obstetrique, 1910, ii.  
*Chambretent*: Soc. de méd. et de chir. de Bordeaux, 1910, viii, 28, ref. Frommels Jahresb., 1910.  
*Collin*: Jour. de méd. de Bordeaux, 1906, iv, 20, No. 17, p. 303-305, ref. Frommels Jahresb., 1906.  
*Corminas*: Rev. de cienc. med. de Barcelona, 1905, xxxi, ref. Frommels Jahresb., 1905.  
*Cramer*: Gyn.-Kongress, Strassburg, 1909; Monatsch. f. Gebrutsh. u. Gynäk., 1914, xxxix.  
*Dutilh*: Med. Weekbl. voor Noord and Zuid, Nederland, 1904, No. 47, ref. Frommels Jahresb., 1904.  
*Fabre*: Lyon méd., 1905, xxxii; Bull. d'acad. de méd., 1905, vi, 6; L'Obstetrique, 1908, p. 25; Ibid., 1910, No. 2.  
*Fabre and Trillat*: Bull. Soc. d'Obstetrique de Paris, 1908.  
*Ferre*: Soc. d'obstet. de Toulouse, 1910, ii, 2; L'Obstetrique, 1910, ii.  
*Funck, Bretano and Roulland*: La Gynec., April, 1913.  
*Genet*: Lyon Méd., 1906, lvi, 273.  
*Girling*: Lancet, London, June, 1912.  
*Goubert*: Bull. et mem. Soc. méd. de Vaucluse, Avignon, 1908, iv, ref. Frommels Jahresb., 1908.  
*Hofbauer*: Arch. f. Gynäk., lxxviii; Zentralbl. f. Gynäk., 1922, No. 15.  
*Lostalot*: Lancet, London, 1913.  
*Lucas-Champonnière*: Jour. de méd. et de chir. prat., lxxxi, 321, ref. Frommels Jahresb., 1910.  
*Masoepuy*: Thèse de Toulouse, 1907.



- Moret*: Bollet. de Col. de med. de Geronne, 1903, viii, 189, ref. *Frommels Jahreshb.*, 1903.
- de Nororche*: Gaz. clin., S. Paulo, 1905, iii, 424; ref. *Frommels Jahreshb.*, 1905.
- Qui*: Echo méd. du nord, Lille, 1904, viii, ref. *Frommels Jahreshb.*, 1904.
- Percerot*: Thèse de Lyon, 1909.
- Pilcer and Ebersson*: Therap. Monatsch., October, 1904.
- Pouz*: Soc. d'obstet. de Toulouse, 1910, ii, 2; L'Obstetrique, 1910, ii.
- Renner*: Mitt. a. d. Grenzgeb. d. Chir., 1905.
- Roland*: Poilu med. Poitiers, 1908, xxiii.
- Romme*: Presse méd., 1904, xi, 23.
- Santi*: Ztschr. f. Geburtsh. u. Gynäk., lxxiv; Folia gyn., v, fasc. 2, p. 231; 16. Kongress d. ital. geburtsh.-gyn. Ges.
- Secheyron*: Soc. d'obstet. de Toulouse, L'Obstetrique, 1910, iii.
- Tello*: Rev. med. de Sevilla, 1908, xxvii, 129, 161, ref. *Frommels Jahreshb.*, 1908.
- Thirolaix*: Bull. méd., 1907, No. 65, ref. *Frommels Jahreshb.*, 1907; Internat. Clin., 1908, i, No. 18, ref. *Frommels Jahreshb.*, 1908.
- Vauters*: Dissertation, Lille, 1909, ref. Zentralbl. f. Gynäk., 1911, p. 725; Thèse de Lille, 1909.
- Vauverts*: Echo méd. du nord Lille, 1909, xiii, No. 9, p. 220, ref. *Frommels Jahreshb.*, 1909.
- Vinagre*: Dissertation, Lisboa, ref. *Frommels Jahreshb.*, 1910.
- Vincent*: Lyon méd., 1906, No. 1.
- Voiturier*: Thèse de Lyon, 1908-1909.

## Protein Therapy

### Vaccination

- Artom di Sant Agenese*: Bolletino R. accademia medica di Roma, 1908, xxxiv, ref. *Frommels Jahreshb.*, 1908.
- Bineund Lissner*: München med. Wehnsehr., 1907, No. 51.
- Bristow*: New York State Jour. Med., March, 1908, ref. *Frommels Jahreshb.*, 1908.
- Burkhardt*: Zentralbl. f. Schweizer Aerzte, 1915, No. 38.
- Burnham*: Ann. Surg., 1914, No. 49.
- Chalmers and O'Farrel*: Jour. Am. Med. Assn., 1916, No. 21, p. 1661.
- Champtaloup*: Brit. Med. Jour., June, 1914.
- Crowe and Wynn*: Brit. Med. Jour., August 8, 1908, ii, 303.
- Cushing*: Am. Jour. Obst., July, lxii.
- Deaver, da Costa and Pfeiffer*: Surg., Gynec. and Obst., August, 1910.
- Gow*: Brit. Med. Jour., 1920, ii, 168.
- Grier*: Brit. Med. Jour., September 30, 1916.
- Grodall*: Canada Med. Assn. Jour., 1914, p. 589.
- Hamm*: Strassburger Gyn.-Kongress, 1909.
- Hartwell, Streeter and Green*: Surg., Gynec. and Obst., September, 1909.
- Hawkjard*: Brit. Med. Jour., January, 1912.
- Heynemann*: 80th Naturforscher Vers. in Köhn.
- v. Jaschke*: Ztsch. f. Geburtsh. u. Gynäk., lxxi, No. 2.
- Jewett*: Am. Jour. Obst., March, 1908, ii, 281.
- Jordan*: Brit. Med. Jour., 1912, vii, 6.
- Köhler*: Wien. gyn. Ges., 1915, vi, 8, ref. Zentralbl. f. Gynäk., 1915, No. 31.
- Kraus and Mazza*: Deutsch. med. Wehnsehr., 1915, No. 39.
- Krömer*: Strassburger Gyn.-Kongress, 1909.
- Lloyd*: Intercolonial Med. Jour. Australasia, 1907, ii, ref. *Frommels Jahreshb.*, 1907.
- MacLeod*: Buffalo Med. Jour., July, 1908, ref. *Frommels Jahreshb.*, 1908.
- Martin*: Strassburger Gyn.-Kongress, 1909.
- Martyn*: Jour. Am. Med. Assn., 1908, i.

- Menger*: Med. Klin., 1912, No. 8.  
*Montgomery*: Surg., Gynec. and Obst., Abst., xix.  
*Müller, E. F.*: München med. Wehnschr., 1919, No. 43; Med. Klin., 1918, No. 28.  
*Murray*: Brit. Med. Jour., 1920, ii, 269.  
*Oastler*: Am. Jour. Obst., April, 1909.  
*Palano*: Ztschr. f. Geburtsh. u. Gynäk., lv.  
*Renand*: Presse méd., 1911.  
*Robbers*: Strassburger Gyn.-Kongress, 1909.  
*Bowlette*: Jour. Obst. and Gynec. Brit. Emp., June, 1912.  
*Schereminskaja*: Wratsch. gaz., 1913, No. 24, ref. Frommels Jahresb., 1913.  
*Schiffmann and Kohn*: Wien. klin. Wehnschr., 1909, No. 3.  
*Schwarz*: Am. Jour. Obst., lxii.  
*Seidel and Högl*: Wien. klin. Wehnschr., 1923, No. 18.  
*Szyli*: Wien. klin. Wehnschr., 1918.  
*Terry*: Post-Graduate, 1910, xxv, 1041, ref. Frommels Jahresb., 1910.  
*Veitsch*: Brit. Med. Jour., April, 1910.  
*Watters and Eaton*: Boston Med. and Surg. Jour., 1911, iv, 13, ref. Frommels Jahresb., 1911.  
*Weaver*: Am. Jour. Med. Sc., September, 1910, cxl, 422, ref. Frommels Jahresb., 1910.  
*Werner*: Wien. Gynäk. Ges., 1915, vi, 8, ref. Zentralbl. f. Gynäk., 1915, No. 31.  
*Western*: Jour. Obst. and Gynec., Brit. Emp., February, 1912.  
*Williams, Cragin, Franklin and Newell*: Tr. Am. Gynec. Soc., Am. Jour. Obst., July, lxii.  
*Wolfsohn*: Berl. klin. Wehnschr., 1911, No. 33.  
*Wolverton*: Jour. Am. Med. Assn., October, 1909.

### Serum

- Anderson*: Lancet, London, 1904, iii, 1211.  
*Arndt*: Petersburger med. Wehnschr., 1910, No. 47; Med. Obozr., 1911, No. 4, ref. Frommels Jahresb., 1911.  
*Arnold*: Am. Jour. Obst. and Gynec., 1922, iv, No. 6.  
*Aronson*: Ber. d. deutsch. pharm. Gesellsch., 1903, xiii, No. 3, p. 73; Ver. f. inn. Med., Berlin, 1904, v, 2; Deutsch. med. Wehnschr., 1904, No. 24; Berl. med. Ges., 1905, ii, 8; Deutsch. med. Wehnschr., 1905, No. 9; Ibid., 1906, No. 34; Ibid., 1909, p. 685; Ibid., 1909, No. 15.  
*Bailey*: Am. Jour. Obst. and Gynec., 1924, vii, No. 6.  
*Bartram*: Zentralbl. f. Gynäk., 1921, No. 15.  
*Bergey*: Pennsylvania Med. Jour., 1903, vii, 7, ref. Frommels Jahresb., 1903, Med. Record, New York, 1903, lxiv, 597; Jour. Am. Med. Assn., 1904, xliii, No. 4, p. 161.  
*Bertrandt and Jegyni*: Medijecyna I Kron. Lek., 1913, No. 42, ref. Zentralbl. f. Gynäk., 1913, p. 1829.  
*Bery*: Med. Record, New York, 1905, lxvii.  
*Bewersdorf*: München med. Wehnschr., 1907, p. 1482.  
*Blackwood*: Lancet, London, 1905, ii.  
*Bleyne*: Limousin méd., Limoges, 1906, xxx, ref. Frommels Jahresb., 1906.  
*Blumenstein*: Rev. gén. de sc. pures et appliq., Paris, 1905, xvi.  
*Boeck*: Dissertation, Halle, 1903.  
*Bohnstedt*: Petersburger med. Wehnschr., 1907, p. 491; Wratsh, No. 13; ref. Zentralbl. f. Gynäk., 1911, p. 1550.  
*Boissard*: Clinique, Paris, 1907, ii.  
*Bolognesi*: Bull. gén. de Thérap., 1906, iii, 30, ref. Frommels Jahresb., 1906.  
*Bouttiau*: Ann. Soc. méd. chir. de Liège, 1903, xliii, 567, ref. Frommels Jahresb., 1903.  
*Briggs*: Brit. Med. Jour., 1904, i, 433.

- Brodhead*: Am. Jour. Obst. Gynec., 1923, v, No. 5.
- Brunet*: Med. Ges. z. Magdeburg, München med. Wehnschr., 1908, No. 20, p. 4069.
- Bumm*: Berl. med. Ges., 1904, vi, 15; Berl. klin. Wehnschr., 1904, No. 44; Berl. med. Ges., 1905, ii, 8; Deutsch. med. Wehnschr., 1905, No. 9.
- Burckhard*: Reichs-Medizinal-Anzeiger, 1905, xxx.
- Burkhardt*: Ztschr. f. Geburtsh. u. Gynäk., liii, No. 3, p. 490; Fränk. Ges. f. Geburtsh. u. Gynäk., 1904, i, 30; ref. Zentralbl. f. Gynäk., 1904, No. 22.
- Burkard*: Arch. f. Gynäk., lxxix, No. 3.
- Burnham*: Ann. Surg., 1914, xlix.
- Busalla*: Berl. klin. Wehnschr., 1906, No. 34.
- Caic*: Brit. Med. Jour., 1903, ii, 1210.
- Cameron*: Brit. Med. Jour., 1907, ii.
- Charles*: Jour. d'accouch., Liège, 1906, xxvii.
- Chatterton*: Indian Med. Gaz., 1906, xli, ref. Frommels Jahresb., 1906.
- Christison*: St. Paul. Med. Jour., 1906, viii, ref. Frommels Jahresb., 1907.
- Coleman*: Old Dominion Jour. Med. and Surg., 1904, ii, 199, ref. Frommels Jahresb., 1904.
- Cornicek*: Texas Med. News, 1904-1905, xiv, 688, ref. Frommels Jahresb., 1905.
- Courmont*: Rev. prat. d'obst. et de gynéc., Paris, 1905, p. 346; Bull. Soc. méd. d. hôp. de Lyon, 1905, iv; Lyon méd., 1905, iv.
- Cressey*: Lancet, London, 1905, i, 487.
- Delbet*: Compt. rend. Soc. de biol., 1904, lvi, 837; Jour. méd. de Paris, 1906, xviii, series 2, p. 203.
- Delmas*: Gynécologie, 1921, ref. Zentralbl. f. Gynäk., 1921, No. 51, p. 1856.
- Dobson*: West London Med. Jour., 1907, xii, 295, ref. Frommels Jahresb., 1907.
- Dopple*: Dissertation, Bon., 1911, ref. Zentralbl. f. Gynäk., 1912, p. 1471.
- Duncan*: Lancet, London, 1904, i, 720.
- Eggel*: Gynäk. Ges. München, 1905, vii, 19, ref. München. med. Wehnschr., 1905, No. 32, p. 1566.
- Eichhorst*: Med. Klin., 1910.
- Erck*: Am. Jour. Obst. and Gynec., 1922, iv, No. 6.
- Falk*: Berl. med. Ges., 1904, vi, 15, ref. Berl. klin. Wehnschr., 1904, No. 44.
- Falkner*: Wien. klin. Wehnschr., 1907, No. 22.
- Fellenberg*: München med. Wehnschr., 1908, No. 27.
- Filia*: Arch. de méd. de Paris, 1905, viii.
- Fisher*: Am. Jour. Obst. and Gynec., 1922, iv, No. 6.
- Foulerton*: Lancet, London, 1904, ii, 1828.
- Fourest*: Jour. de sages-femmes, 1906, xxxiv, ref. Frommels Jahresb., 1906.
- Freund*: Berl. med. Ges., 1904, vi, 15, ref. Berl. klin. Wehnschr., 1904, No. 44; Handb. d. Serumtherapie v. Wolff-Eisner, 1910.
- Fromme*: Jüchen med. Wehnschr., 1906, No. 1.
- Fuchs*: Gynäk. Ges. Breslau, 1910, ii, 15, ref. Zentralbl. f. Gynäk., 1910.
- Füth*: Monatschr. f. Geburtsh. u. Gynäk., xxv, 263, (Sitzungsber).
- Funck*: Jour. méd. de Bruxelles, 1904, viii, 847.
- Funck-Brentano and Roulland*: La Gynécologie, April, 1913.
- Gammel*: Brit. Med. Jour., 1904, i, 433.
- Ginzetti*: Riforma med., 1903, xix, No. 45.
- Girling*: Lancet, London, June, 1912.
- Grochtmann*: Deutsch. med. Wehnschr., 1904, No. 10.
- Grünbaum*: Brit. med. Jour., 1904, i, 433.
- Haase*: Gynäk. Ges. z. Breslau, 1910, ii, 15, ref. Zentralbl. f. Gynäk., 1910.
- Hagemann*: 39. Versammlg. d. deutsch. Ges. f. Chir., 1910, ref. München med. Wehnschr., 1910, No. 17.
- Hamilton*: Am. Jour. Obst., 1904, 1, 589.
- Hanel*: Therapist, London, 1903, lxxiv, ref. Frommels Jahresb., 1903, Deutsch. med. Wehnschr., 1905, No. 45.

- Hannah*: Am. Jour. Obst. and Gynec., 1922, iv, No. 6.
- Heimann*: Med. Klin., 1913, No. 34, Ztschr., f. Geburtsh. u. Gynäk., lxxi, No. 3.
- Heynemann*: Strassburger Gyn-Kongress, 1909; Vereinigung. mittel-deutsch. Gynäk., Halle, 1909, Jänner, ref. Zentralbl. f. Gynäk., 1909, p. 39.
- Hirst*: Jour. Am. Med. Assn., 1914, lxii, 1873.
- Hoffmann*: Deutsch. med. Wehnschr., 1904, No. 46, p. 1686.
- Hofmeier*: Fränk. Ges. f. Geburtsh. u. Gynäk., 1904, i, 30; ref. Zentralbl. f. Gynäk., 1904, No. 22.
- Howard*: St. Barth. Hosp. Jour., London, 1904, lxxi, ref. Frommels Jahresb., 1904.
- Hunton*: Am. Jour. Obst. and Gynec., 1924, vii, No. 6.
- Hynes*: Brooklyn Med. Jour., 1905, xix, 311, ref. Frommels Jahresb., 1905.
- Impastato*: Gaz. sicil. di med. e chir., 1903, No. 28, p. 468, ref. Frommels Jahresb., 1903.
- Jakoby*: Zentralbl. f. d. ges. Therap., 1907, xxv.
- James*: Hahneman Monthly, 1914, p. 809.
- Jaworsky*: Gaz. lek., 1907, No. 28, ref. Zentralbl. f. Gynäk., 1908, p. 1455.
- Jayle*: Presse méd., 1905, xi, 8.
- Jones*: Brit. Med. Jour., 1903, ii, 1210; Australasia Med. Gaz., 1904, xxiii, 61, ref. Frommels Jahresb., 1904.
- Karewsky*: Ver. f. inn. Med., Berlin, 1904, v, 2; Deutsch. med. Wehnschr., 1904, No. 24.
- Klein*: Berl. med. Wehnschr., 1905, No. 3.
- Koblanck*: Ztschr. f. ärztl. Fortbild., 1912, No. 13.
- Kolle, Sachs and Georgi*: Deutsch. med. Wehnschr., 1918, No. 10.
- Kozicki*: Gynekologja, 1904, No. 2 (polnisch), ref. Frommels Jahresb., 1904.
- Krongold-Vinaver*: Ann. de l'institut Pasteur, 1921, xxxv, No. 12; Bull. de la d'obstet. et de Gynec. de Paris, 1921, x, No. 2.
- Landau*: Berl. med. Ges., March, 1909, ref. Berl. klin. Wehnschr., 1909, p. 685.
- Larned*: Illinois Med. Jour., 1905, viii, 121, ref. Frommels Jahresb., 1905; Therap. Gaz. 1905, xxxi, ref. Frommels Jahresb., 1905.
- Leary*: Intercolonial Med. Jour. Australasia, 1905, x, ref. Frommels Jahresb., 1905.
- Leith Murray*: Practitioner, 1912.
- Leo*: Med. Ges. z. Magdeburg, 1908, ref. München med. Wehnschr., 1908, p. 1069.
- Lewis*: Clin. Rev., Chicago, 1906-1907, xxiv, ref. Frommels Jahresb., 1907.
- Longyear*: Jour. Michigan Med. Soc., 1903, ii, 270, ref. Frommels Jahresb., 1903.
- Lotsch*: Med. Ges. z. Magdeburg, 1908, ref. München. med. Wehnschr., 1908, p. 1069.
- Lubowsky*: All. med. Centr.-Ztg., 1905, lxxiv, 913; Therapist, London, 1906, xvi, ref. Frommels Jahresb., 1906.
- Mackenzie and Blandy*: Lancet, London, 1903, ii, 884.
- Mager*: Beitr. z. Geburtsh. u. Gynäk., 1908, xii, No. 2.
- Mainzer*: Deutsch. med. Wehnschr., 1903, No. 50, p. 955.
- Marmorek*: Berl. med. Ges., 1905, ii, 8; Deutsch. med. Wehnschr., 1905, No. 9.
- Martin, E.*: Berl. klin. Wehnschr., 1906, No. 29.
- Masson*: Rev. prat. d'obst. et de paediat., 1913, No. 290, ref. Zentralbl. f. Gynäk., 1913, p. 1829.
- Mazer*: Am. Jour. Obst. and Gynec., 1922, iv, No. 6.
- Mazzei*: Riforma med., 1908, xxiv, No. 28.
- Meissl*: Wien. klin. Wehnschr., 1909, No. 1.



- Menzel:** Ver. f. inn. Med., Berlin, 1903, iii, 23; Deutsch. med. Wehnschr., 1903, No. 25, p. 439; Diskussion hiezu Vereinsbeilage, No. 17, p. 131; München. med. Wehnschr., 1903, Nos. 25 and 26; Ver. f. inn. Med. Berlin, 1904, v, 2; Deutsch. med. Wehnschr., 1904, No. 24; Wien. klin. Wehnschr., 1904, No. 44; Berl. Klin., 1906, xviii; Vereinigung Mitteldeutsch. Gynäk., Halle, 1909, ref. Zentralbl. f. Gynäk., 1909, p. 391.
- Meyer, F.:** Ztschr. f. diätet. u. physik. Therap., 1903; Ztschr. f. klin. Med., 1, Nos. 1 and 2; Ver. f. inn. Med., Berlin, 1904, v, 2; Deutsch. med. Wehnschr., 1904, No. 24, p. 898; Berl. med. Ges., 1905, ii, 8; Berl. klin. Wehnschr., 1905, No. 8, pp. 197, 216; Diskussion, Deutsch. med. Wehnschr., 1905, No. 9; Therap. d. Gegenw., 1906, xlvii, 32, 77.
- Meyer and Michaelis:** Berl. klin. Wehnschr., 1903, No. 16, p. 377; München med. Wehnschr., 1903, No. 12, p. 538.
- Meyer and Ruppel:** Med. Klin., 1907, p. 1192.
- Müller:** Jour. Michigan Med. Soc., 1903, ref. Frommels Jahresb., 1903.
- Montanelli:** La Ginecologia, Firenze, viii, No. 47.
- Morgan:** Brit. Med. Jour., 1904, i, 433.
- Müller:** Med. Ges. z. Magdeburg., 1908, ref. München med. Wehnschr., 1908, p. 1069.
- Murtry:** Lancet, London, 1906, ii, 809.
- Neisser and Guernini:** Arb. a. d. k. Inst. f. exper. Therap. in Frankfurt, 1908, No. 4.
- Neufeld and Rimpau:** Deutsch. med. Wehnschr., 1904, No. 40.
- Olshausen:** Berl. med. Ges., 1904, vi, 15, Ref. Berl. klin. Wehnschr., 1904, No. 44.
- Opfer:** Deutsch. med. Wehnschr., 1904, No. 33, p. 1211.
- Orgle:** Lancet, London, 1904, i.
- Parkinson:** Lancet, London, 1906, i, 1280.
- Parrot:** Carolina Med. Jour., 1905, lii, 87, ref. Frommels Jahresb., 1905.
- Paton:** Med. Press and Circ., 1906, lxxxi, 119, 145.
- Pease:** Med. Rev., New York, 1905, xi, 797; Am. Med., 1905, x, 480, ref. Frommels Jahresb., 1905.
- Peham:** Wien. klin. Wehnschr., 1904, No. 15; Arch. f. Gynäk., lxxiv.
- Petit:** Rev. de gynec. et d'obstet., 1904, No. 3, p. 498; Med. Record, New York, 1907, lxxi.
- Petit, Barlerin and Demelin:** Bull. Soc. d'obstet. de Paris, 1906, ix, No. 2.
- Petruschky:** Deutsch. med. Wehnschr., 1906, No. 42.
- Pfeiffer:** Ost-u. westpreuss. Ges. f. Gynäk., 1906, v, 19; Deutsch. med. Wehnschr., 1906, No. 42; Vereinsbeilage, p. 1722.
- Piasetzka:** Arch. de méd. expér. et d'anat. path., Paris, 1903, xv, 589, ref. Frommels Jahresb., 1903.
- Pilczner and Ebersson:** Therap. Monatsch., October, 1904.
- Pinard:** Budapestern intern. med. Kongress, 1909, ref. Zentralbl. f. Gynäk., 1909.
- Pinkuss:** Ver. f. inn. Med., Berlin, 1904, v, 2; Deutsch. med. Wehnschr., 1904, No. 24.
- Popescu and Georgescu:** Rev. scintelor medicale, July and August, 1907, ref. Zentralbl. f. Gynäk., 1908, p. 360.
- Porter:** Lancet-Clinic, 1905, liv, 405, ref. Frommels Jahresb., 1905.
- Raw:** Jour. Obst. and Gynec. Brit. Emp., 1904, v, No. 4, p. 334; Brit. Med. Jour., 1904, i, 433; Med. Press and Circ., 1905, lxxx; Liverpool Med. Chir. Jour., Jänner, 1905, ref. Frommels Jahresb., 1905; Brit. Med. Jour., June, 1910.
- Reno:** Pommersche gyn. Ges., 1905, viii, 13, ref. Monatschr. f. Geburtsh. u. Gynäk., xxii, 710.
- Rose:** Lancet, London, 1904, ii, 1830.
- Rothrock:** St. Paul Med. Jour., 1909, No. 12, ref. Zentralbl. F. Gynäk., 1910, p. 895.
- Roussel:** New Orleans Med. and Surg. Jour., November, 1908; ref. Frommels Jahresb., 1908.

- Rubeska*: Lék. rozhledy, ref. Zentralbl. f. Gynäk., 1913, p. 130.
- Ruppelt*: Med. Klin., 1905, i, Nos. 27 and 28.
- Schäfer*: Zentralbl. f. Gynäk., 1918, No. 8, p. 148.
- Schäffer*: Der prakt. Aerzt. Leipzig, 1907, xlvii, 6, 33.
- Schapiro*: Praktitscheskii Wratsch, 1908, No. 30, ref. Frommels Jahreshb., 1908.
- Schauenstein*: Bruns Beitr. z. klin. Chir., lxvii.
- Schmidt*: Med. Record, New York, 1905, iv, 15.
- Schultze*: Med. Klin., 1906, No. 42.
- Schwabland*: Java Med. Jour. des Montes, 1903, ix, 178, ref. Frommels Jahreshb., 1903.
- Seel*: Ztschr. f. ang. Mikr., 1903, xi, 195.
- Simon*: Zentralbl. f. Bakteriologie, Part 1, xlv; Fränk. Ges. f. Geburtsh. u. Gynäk., 1904, i, 30; ref. Zentralbl. f. Gynäk., 1904, No. 22.
- Smyth*: Brit. med. Jour., 1907, iii, 2.
- Sommersted*: Zentralbl. f. Bakteriologie, 1903, Part 1, No. 9, p. 722.
- Spencer*: Lancet, London, 1904, i, 158.
- Spassky*: Russ. med. Rundschau, Berlin, 1903, p. 790, ref. Frommels Jahreshb., 1903.
- Stadelmann*: Ver. f. inn. Med., Berlin, 1904, v, 2; Deutsch. med. Wehnschr., 1904, No. 24.
- Stafford*: Jour. Michigan State Med. Soc., 1908, ref. Frommels Jahreshb., 1908.
- Stanger*: Lancet, London, 1906, ii, 654.
- Steinhauser*: Deutsch. med. Wehnschr., 1903, No. 12, p. 213.
- Stone*: Surg., Gynec. and Obst., 1912, No. 1.
- Sutherland*: Deutsch. med. Wehnschr., 1903, No. 12, p. 213.
- Tavel*: Deutsch. med. Wehnschr., 1903, Nos. 50 and 51; Zentralbl. f. Bakteriologie, xxxiii, 1.
- Thalheimer and Hogen*: Am. Jour. Obst. and Gynec., 1923, vi.
- Thirion*: Jour. d. sc. méd. de Lille, 1903, ii, 543, ref. Frommels Jahreshb., 1903.
- Thorn*: Med. Ges. z. Magdeburg., 1908, ref. München med. Wehnschr., 1908, p. 1069.
- Trucidale*: Lancet, London, 1906, ii, 809.
- Veiga*: Rev. med. d. Uruguay, Montevideo, 1903, vi, 363, ref. Frommels Jahreshb., 1903.
- Wagner, P.*: Frauenärzte, 1906, xxi.
- Wainwright*: Internat. Clinic, 1905, iii, 84, ref. Frommels Jahreshb., 1905.
- Walther*: Ztschr. f. Geburtsh. u. Gynäk., li, No. 3, p. 469.
- Waters*: Therapist, London 1906, xvi, 69, ref. Frommels Jahreshb., 1906.
- Weirick*: Med. Visitor, 1903, xix, 5, ref. Frommels Jahreshb., 1903.
- Weißling*: Dissertation, Berlin, 1910, ref. Frommels Jahreshb., 1910.
- Wendel*: Med. Ges. z. Magdeburg, 1908, ref. München med. Wehnschr., 1908, p. 1069.
- Willard*: Vermont Med. Monthly, 1905, xi, 157, ref. Frommels Jahreshb., 1905.
- Williams*: Am. Jour. Obst. and Gynec., 1922, iv, No. 6.
- Withe*: Med. Rec., New York, 1903, lxiii, 55.
- Wolff*: Berl. med. Ges., 1905, ii, 8; Deutsch. med. Wehnschr., 1905, No. 9.
- Wright*: Jour. Am. Med. Assn., 1906, xlvii, 1505.
- Zangemeister*: Monatschr. f. Geburtsh. u. Gynäk., xxvi; Deutsch. med. Wehnschr., 1906, No. 42; Ibid., 1906, No. 47; München med. Wehnschr., 1908, No. 16; Prakt. Ergebn., ii, No. 1; Berl. klin. Wehnschr., 1909, No. 20; Strassburger Gyn.-Kongress, 1909; 82. Versammlg. deutsch. Naturf. u. Aerzte z. Königsberg, 1910, ref. Zentralbl. f. Gynäk., 1910, p. 1421; Berl. klin. Wehnschr., 1910, No. 43.

## Different Remedies

- Abadie:** Gaz. d. hôp. de Lyon, 1903, iv, 361.
- Anderodias:** Gynec. et. obstet., 1921, iv, v, (Uterine lavage with Dakin-Carrel solution.)
- Audebert:** Thèse de Paris, 1904. (Yeast.)
- Aumond:** Thèse de Paris, 1904. (Iodine.)
- Bekers:** Jour. Belge de gynec., January, 1914, ref. Frommels Jahresb., 1914. (Lactic acid bacillus.)
- Bins:** Zentralbl. f. Gynäk., 1903, No. 23. (Alcohol.)
- Bogodurov:** Jour. Akush. i. Zhensk. Boliez., 1907, No. 1-9, ref. Zentralbl. f. Gynäk., 1908, p. 412.
- Brindeau:** Bull. de soc. d'obstet. de Paris, 1908, xi, 158.  
(Lactic acid bacillus): Arch. mens. d'obstet. et de gyn., March, 1912, ref. Zentralbl. f. Gynäk., 1912, p. 1740.
- Burford:** Lancet, London, 1905, i.
- Burford and Johnston:** Brit. Gynec. Jour., August, 1905, p. 104.
- Cabanes:** Bull. méd. de l'Algérie, 1906, xviii, ref. Frommels Jahresb., 1906, (Iodine.) Med. Press and Circ., 1906, lxxxvii, ref. Frommels Jahresb., 1906.
- Cabot:** Boston Med. and Surg. Jour., 1903, vii, 23. (Alcohol.)
- Carruthers:** Brit. Med. Jour., 1908, i. ( $H_2O_2$ .)
- Charles:** Jour. d'accouch., Liège, 1904, ix, 25. (Sulphate of Quinine.)
- Craigs:** New Zealand Med. Jour., 1904, iii, ref. Frommels Jahresb., 1904. (Diphtheria-Antitoxin.)
- Cramer:** Monatschr. f. Geburtsh. u. Gynäk., 1914, No. 6; Sitzungsber. d. niederrhein-westphäl. Ges. f. Gynäk. u. Geburtsh., 1914, iii, 1, ref. Zentralbl. f. Gynäk., 1914, p. 876. (Turpentine.)
- Daniel and Costa:** Gaz. d. hôp., 1912, No. 103, ref. Zentralbl. f. Gynäk., 1913, p. 294. (Iodine vapor.)
- Deacon:** Med. Rec., New York, lxxvii, 64. (Diphtheria-Antitoxin.)
- Delmas:** Rev. mens. de gynéc., d'obstét. et de pédiat., November, 1913, (Turpentine oil gauze.)
- Deslandes:** Bull. Soc. d'obstet. de Paris, 1903, vi, No. 2, p. 107. ( $H_2O_2$ .)
- Doederlein:** Internat. Gyn.-Kongress, London, 1913, ref. Zentralbl. f. Gynäk., 1913, p. 1433. (Roentgen.)
- Drenkhahn:** Therap. Monatsch., February, 1905. (Atropine, 0.0005 g.)
- Dupont:** Ann. de gynec. et d'obst., July, 1910, vii. (Hot air treatment of puerperal ulcers.)
- Editorial,** Med. Rec., New York, 1903, lxiii, 468. (Alcohol.)
- Eisenreich:** Zentralbl. f. Gynäk., 1910, No. 14.
- Elsässer:** Deutsch. med. Wehnschr., 1908, No. 58. (Iodine.)
- Ercklentz:** Therap. d. Gegenw., 1903.
- Fick:** Korrespondenzbl. f. Schweizer Aertze, 1904, p. 158. (Alcohol.)
- Fischer:** Med. Klin., 1910, No. 3.
- Foucon:** Thèse de Lille, 1906. (Nucleinic acid.)
- Funck-Brentano:** Ann. de gynéc. et d'obst., 1908, No. 1. (Hydrogen peroxide lavage.)
- Hahn:** Prager med. Wehnschr., 1913, No. 36.
- Hare:** Assn. Am. Phys., Med. Rec., New York, 1903, lxiii, 916. (Alcohol.)
- Harrar:** Jour. Am. Med. Assn., September, 1911, (General Measures); Am. Jour. Obst., lxviii, 828, (Magnesium Sulphate).
- Haward:** Lancet, London, 1906.
- Hellendahl:** Zentralbl. f. Gynäk., 1921, No. 45, (Dakin solution).
- Hermstein:** Zentralbl. f. Gynäk., 1921, No. 19, (Injections of Turpentine).
- Hiss and Zinser:** Jour. Med. Research, 1908, ix, 323, (Experimental Work with Leucocytic Extracts and Exudates).
- Holzbauer:** Beitr. z. Geburtsh. u. Gynäk., x, 542, (Nucleinic acid); Arch. f. Gynäk., lxviii, 359, (Nucleinic acid); Zentralbl. f. Gynäk., 1922, No. 15, (Nucleinic acid and Hypophyseal Extract).

- Holitscher:** Prager med. Wehnschr., 1903, No. 31-33, (Alcohol).
- Hornstein:** Jour. Akush. I. Zhensk. Boliez., April, 1904, ref. Frommels Jahresb., 1904.
- Huggins:** Surg., Gynec. and Obst., x, 642.
- Hume:** ref. Zemaine méd., 1903, No. 48, p. 396.
- Jakobs:** Internat. Gyn.-Kongress, London, 1913, ref. Zentralbl. f. Gynäk., 1913, p. 1433. (Roentgen.)
- Jeannin:** Ann. de gynéc. et d'obstet., 1909, vi, (Bacterium Lactate).
- Jekewitsch:** Ref. Zentralbl. f. Gynäk., 1913, p. 1399.
- Jungbluth:** Dissertation, Bonn, 1902.
- Kahrs:** Med. Revue, Bergen, xxviii, 178.
- Keim:** Jour. d. sages-femmes, 1913, (Aminal Liver for Thrombophlebitis).
- Klotz:** Monatschr. f. Geburtsh. u. Gynäk., xxxvi, Erg.-H., (Pituitrin).
- Komor:** Ungar. med. Presse, 1904, ix, 115-133.
- Kramer:** Med. Ges. Kiel, Sitzg., 1911, ii, 2. (Iodine.)
- Kroemer:** Zentralbl. f. Gynäk., 1906, No. 4, (Bier's suction).
- Krohl:** Berl. klin. Wehnschr., 1913, No. 42. (Mercury.)
- Kuhn:** Normandie méd., 1904, xix, 44, ref. Frommels Jahresb., 1904. (Quinine.)
- Lambert:** New York Acad. of Med. Rec., 1903, lxiv. (Alcohol.)
- Lambinon:** Arch. de Méd. des enfants, October, 1904. (Iodine.)
- Legendre:** Presse méd., 1903, No. 87, p. 763. (Alcohol.)
- Macan:** Jour. Obst. and Gynec., Brit. Emp., 1908, cxxvi.
- Maclachan:** Brit. Med. Jour., July 12, 1911, ref. Zentralbl. f. Gynäk., 1912, p. 515. (Niemeyer Mixture.)
- MacKay:** Am. Jour. Obst., October, 1907, lvi.
- Marchet:** Gaz. d. hôp., 1905, No. 13. (Stabilization for Phlebitis.)
- Margnie:** Gaz. d. hôp., ex., (Fowler's position); Jour. Méd. et de chir. prat., 1910, No. 18; Jour. d. sages-femmes, 1913.
- Martel:** L'Obstetrique, 1911, iii, 836.
- Martinet:** Presse méd., 1903, No. 10, p. 145. (Alcohol.)
- Martinez:** Crón. méd. mexicana, 1906, ix; Rev. Ibero-Am. de cien. méd., 1906, xv, ref. Frommels Jahresb., 1906. (Iodine.)
- Mas de Xaras:** Bol. mes. d. Col. de méd. de Gerona, xv, ref. Frommels Jahresb., 1910. (Iodine.)
- Miyake:** Mitt. a. d. Grenzgeb. d. Med. u. Chir., xiii, No. 4, p. 904. (Nucleinic acid.)
- Monro and Findlay:** Glasgow Med. Jour., May, 1904. (Alcohol.)
- Mougeot:** Arch. gén. de méd., 1906, i.
- Noire:** Presse méd., 1920, No. 37.
- Ortali:** Gazz. degli ospedali e delle clin., November, 1908. (Iodine tincture, hot,  $H_2O_2$ .)
- Osborne:** Jour. Am. Med. Assn., 1903, xii, 5.
- Ovary:** Pest med.-chir. Presse, 1904, xl; Semaine méd., 1904, ix, 14.
- Percerot:** Dissertation, Lyon, 1909, ref. Zentralbl. f. Gynäk., 1910, p. 639.
- Persenaire:** New Tijdsr. voor Geneesk., i, 2032, ref. Frommels Jahresb., 1911. (General Treatment.)
- Pilliere:** Gaz. d. hôp., 1906, lxxix, No. 7.
- Pollak:** Arch. f. Gynäk., lxxix, No. 2. (Nucleinic acid.)
- Polnaru-Caplessu:** Chir. Ges. Bukarest, Sitzung, 1908, i, 16, Zentralbl. f. Gynäk., 1908, No. 44, p. 1457.
- Porrit:** Brit. Med. Jour., May 20, 1916, p. 707, (Complex drainage).
- Presta and Tarruella:** Gaz. med. Casalana, Barcelona, 1903, iii, 15, ref. Frommels Jahresb., 1903.
- Pryor:** New York Med. Jour., 1903, lxxviii, No. 8. (Iodine.)
- Queissner:** Strassburger Gyn.-Kongress, 1909 (Traction on portio).
- Benner:** Mitt. a. d. Grenzgeb. d. Med. u. Chir., xv, Nos. 1 and 2.
- Reynier:** Bull. Acad. de méd., 1908, lx; Jour. méd. de Paris, March, 1908. (Oxygen.)



- Beidel*: Med. Klin., 1909, p. 1921.
- Riss*: Marseille méd., 1908, xiv (Iodine); Rev. mens. de gynéc., d'obstét., et de pédiat., 1908, iii. (Iodine.)
- Robins*: Charlotte Med. Jour., 1908, xxxii, ref. Frommels Jahreshb., 1908. (Iodine.)
- Rosenblüt*: Jour. Akush. i Zhensk. Boliez., Febraury, 1911 (russ.), Frommels Jahreshb., 1911.
- Ruth*: Am. Jour. Obst., 1908, lvii.
- Sajus*: Month. Cycl. and Med. Bull., December, 1911, ref. Zentralbl. f. Gynäk., 1912, p. 1295. (Adrenalin.)
- Sarwey*: Strassburger Gyn.-Kongress, 1909. (Iodine.)
- Schottmüller*: München med. Wehnsehr., 1911, No. 39, p. 2051.
- Seeligmann*: Deutsch. med. Wehnsehr., 1908, No. 46, p. 1976. (Naturf.-Vers. Köln; Passive Congestion by Suction.)
- Sick*: Zentralbl. f. Chir., 1908, No. 31 (Iodine).
- Signorel*: Semaine méd., 1905, ii, 22 (Reduction of Chlorides).
- Sitzenfrey*: Monatsehr. f. Geburtsh. u. Gynäk., xxxii, No. 3 (Suction Treatment).
- Somers*: Western Med. Rev., 1904, ix, 79. (Iodine.)
- Steward*: Lancet, London, 1909, i.
- Stone*: Med. Record, New York, 1907, lxxi. (Open air Treatment.)
- Tourneno*: Semaine gynéc., 1904, ix, 177.
- Trillat*: Lyon méd., 1921, cxxx, No. 17, (Dakin's Solution).
- Vaguez*: Soc. de l'Intern. des hôp. de Paris, 1905, vii, 27; Arch. gén. de méd., 1905, No. 31, p. 1979. (Stabilization of limbs without splint for phlebitis.)
- Wernitz*: Wratsch, 1911, No. 49, ref. Frommels Jahreshb., 1911.
- Weydlich*: Korrespondenzbl. d. Ver. deutsch. Aertze in Reichenberg, 1903, xvi, No. 4. (Nuclein-Salt.)
- Wohlgemuth*: Therap. Monatsch., September, 1900. (Intravenous Oxygen.)
- Young*: Moston Med. and Surg. Jour., 1905, cliii, No. 7, p. 212.
- Young*: Brit. Med. and Surg. Jour., 1916, No. 18, p. 633. (Perineal Wound Treatment.)
- Young and Williams*: Boston Med. and Surg. Jour., 1912, iii, 14, ref. Frommels Jahreshb., 1912. (Open air Treatment.)



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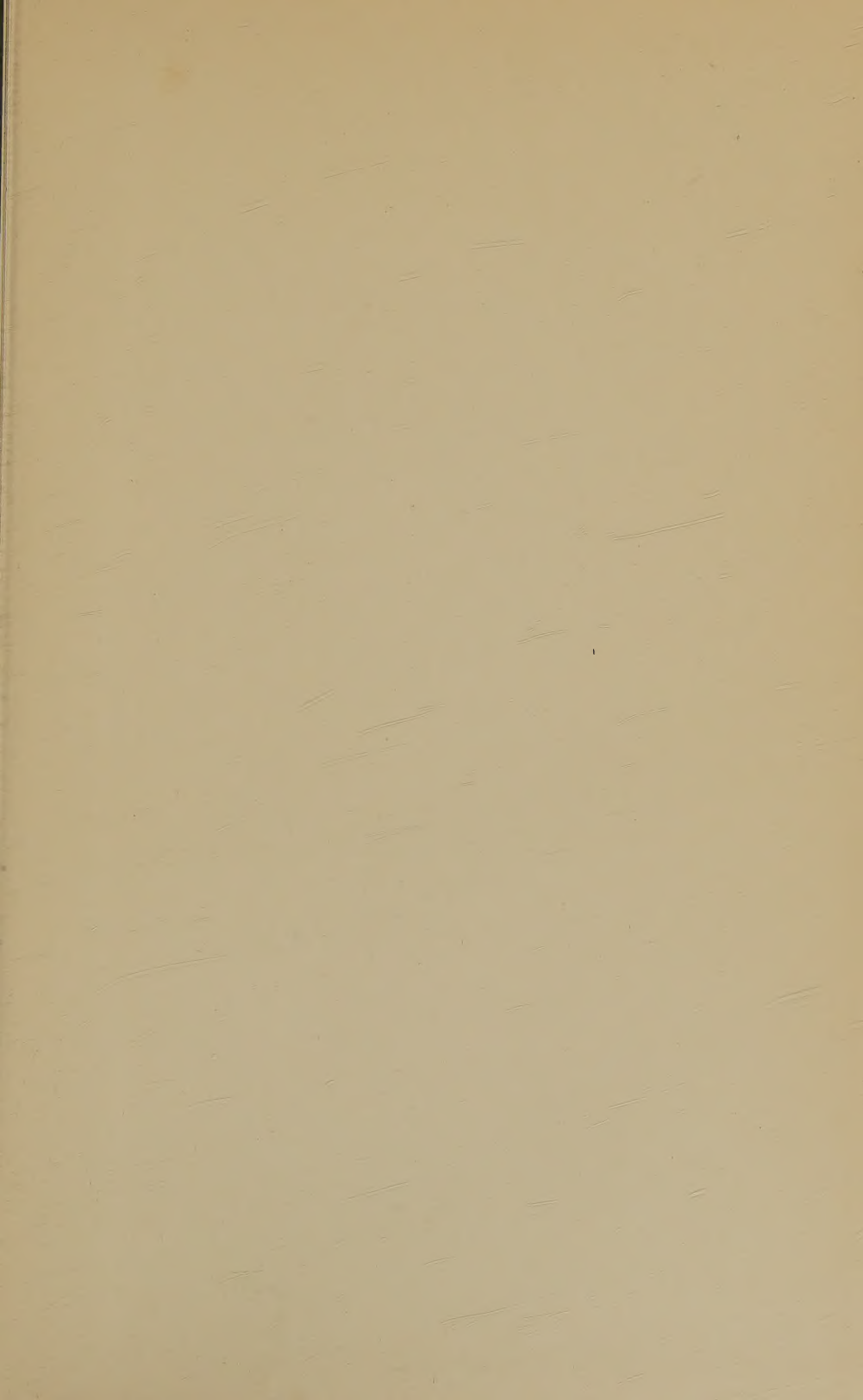
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